XXIII Giornata della Chimica dell'Emilia Romagna 2024

La chimica per le sfide future

ATTI DEL CONVEGNO

giovedì 19 dicembre 2024

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LEZIONI PLENARIE

PL1: FROM IDEA TO PROCESS: BIO-ALCOHOLS FOR THE DEVELOPMENT OF THE BIO-REFINERY CONCEPT

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ABSTRACT

Over the past two decades, applications of bio-alcohols as platform chemicals have aroused new interest because of both environmental concerns connected with petrochemical processes and new economic opportunities seen in bio-based feedstocks. Indeed, bio-ethanol has been demonstrated to be a promising and "green" reactant for both fuels and chemicals, particularly when derived from non-food crops and lignocellulosic materials (second-generation biomass). For example, a common way to convert ethanol into chemicals is by upgrading it over mixed-oxide catalysts with either basic features or bifunctional acid-basic features. This method makes it possible to obtain important chemicals such as 1-butanol (via Guerbet reaction) and 1,3-butadiene (via Lebedev reaction and Ostromisslensky reaction). These two compounds can also be the reactants for other transformations, for example both 1-butanol and butadiene being convertible, amongst others, to maleic anhydride by means of a vanadyl pyrophosphate catalyst. Also, in the field of bio-fuels ethanol is considered one of the most promising building-block. Various catalytic, multi-step processes and technologies have been proposed in recent years for the transformation of the alcohol into mixtures of hydrocarbons, with properties suitable for the use as jet fuel.
An overview of technologies recently investigated for the valorisation of bio-alcohols into chemicals and jet-fuel will be presented, with a highlight on catalyst multifunctional properties needed in order to selectively accelerate the sequential reaction steps needed. Main focus will be on the production of bio-butadiene, the monomer for rubber, and on gasoline/jet-fuel mixtures [1-5]. The technologies described were studied with the aim of increasing the TRL from validation in the laboratory to that in an industrially relevant environment. Industrial companies were involved that supported the research, both from a financial and technological point of view.

REFERENCES

[1] A. Gagliardi et al, Appl. Catal. B, 349 (2024) 123865
[2] D. Cespi et al, Green Chem. 18 (2016) 1625
[3] J. Velasquez et al., Green Chem. 18 (2016) 1653
[4] T. Tabanelli et al., WO 2023/157041
[5] J. Velasquez et al, US 2022/0339610 A1

PL2: SOSTENIBILITA' NELLA PRODUZIONE DI PRINCIPI ATTIVI: CONCETTI E STRATEGIE APPLICABILI NEL SETTORE GENERICO

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ABSTRACT

Il concetto di sostenibilità è oggigiorno alla base di tutto il settore chimico, partendo dal petrochimico ed arrivando fino al farmaceutico. E' proprio quest'ultimo ambito che registra i quantitativi maggiori di rifiuti prodotti per chilo di principio attivo (API) prodotto, arrivando a valori di *Process Mass Intensity* (PMI) superiori a 1000 chili di scarto per chilo di API [1]. Inoltre, la complessità chimica che sottende i processi produttivi farmaceutici richiede l'adozione di una vasta gamma di reagenti e solventi, tra cui diversi considerati ormai conclamate problematiche per l'ambiente e la salute. Sostituire queste sostanze con alternative più sostenibili è l'obbiettivo di tutte le aziende farmaceutiche, con il target ultimo di eliminarle completamente.
La presentazione in oggetto si focalizzerà nel mondo della produzione di farmaci generici attraverso alcuni esempi sviluppati nei nostri laboratori [2,3], elaborando le complessità tecniche e regolatorie che sottendono allo sviluppo di nuove vie di sintesi e quelle collegate a cambi di processo produttivo già registrati.

REFERENCES

[1] Process Mass Intensity Metric – ACS GCI Pharmaceutical Roundtable
[2] Fantoni T. et al. Green Chem., 2024, 26:10929
[3] Bozza D. et al. J. Chrom. A. 2024, 1713:464530

PL3: LA SFERA DI CRISTALLO: APPUNTI DI CHIMICA PER IL TERZO MILLENNIO

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ABSTRACT

This lecture is a personal perspective on some of the key concepts which Chemistry can contribute to shape the future of the planet.
In the present lecture, I will highlight three concepts that can be considered among the key factors that will drive chemical research in the next future, and I will present examples of some of our recent results obtained in these fields.

The vision presented in the lecture will be based on the point of view of a crystallographer, and the examples will span many facets of solid state chemistry, inspired by the principles of crystal engineering, a powerful tool to design materials with high technological added value to address health and environment protection through mild and nature friendly components and methods.

Examples will include (Figure 1): the structural characterization of the arrangement of guest molecules inside the pores of MOFs, to elucidate the uptake and release mechanism [1,2]; the formulation of a predictive model to inspect molecular pairs suitable for cocrystallization [3]; the use of mechanochemistry as a powerful method to develop new materials [4].

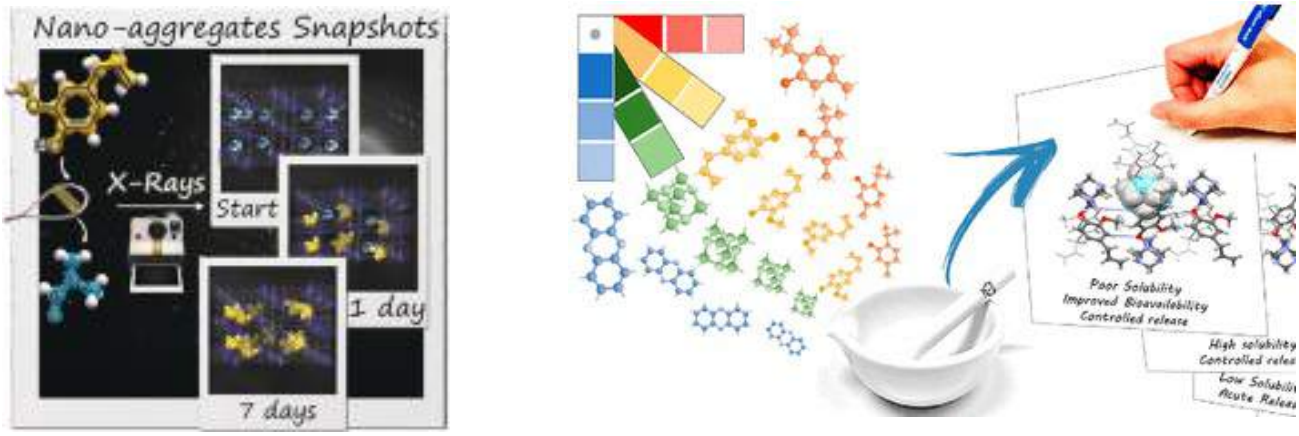

Figure 1. Some aspects of chemistry involved in the development of sustainability. Left: snapshot of nanoaggregates inside MOFs; right: design and mechanochemical synthesis of cocrystals.

REFERENCES

[1] D. Balestri, P. P. Mazzeo, C. Carraro, N. Demitri, P. Pelagatti, A. Bacchi, *Angew. Chem. Int. Ed.* 2019, **58**, 17342–17350
[2] D. Balestri, P.P. Mazzeo, R. Perrone, F. Fornari, F. Bianchi, M. Careri, A. Bacchi, P. Pelagatti *Angew. Chem. Int. Ed*., 2021, **60**, 10194-10202
[3] F. Fornari, F. Montisci, F. Bianchi, M. Cocchi, C. Carraro, F. Cavaliere, P. Cozzini, F. Peccati, P.P. Mazzeo, N. Riboni, M. Careri, A. Bacchi *Chemometrics And Intelligent Laboratory Systems,* 2022*,* **226** 104580-104612
[4] G. I. Lampronti, A. A. L. Michalchuk, P. P. Mazzeo, A. M. Belenguer, J. K. M. Sanders, A. Bacchi, F. Emmerling, *Nat Commun*, 2021, **12**, 6134

PL4: CHEMISTRY MEETS ART: 3D PVC DECORATIONS

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ABSTRACT

PriXel is a patented technology for three-dimensional decoration of PVC surfaces, developed through inkjet printing of a liquid PVC on profiles for doors, windows, and other fixtures. With this process, printed PVC layers fully integrate with the substrate, creating a unified decorative material with three-dimensional reliefs. This technique does not replace existing decorative solutions, such as films and wood-effect coatings, but introduces a new, complementary option. PriXel offers unique durability and customization potential, paving the way for a dedicated market.

Sustainability is a core aspect of PriXel. The system is designed to recover volatile components expelled during the process, condensing them for potential reuse, thus significantly reducing environmental impact compared to conventional coating methods, where volatile components are often dispersed into the environment. Additionally, the use of recycled PVC from industrial waste is being explored to further enhance its circular approach.

PriXel was developed by Graf Industries, within its research and development division, Graf Inventa, which has brought together expertise in mechanics, electronics, software, and chemistry to realize a completely new technology. Current research focuses on expanding the color range, aiming to achieve a four-color system for increased decorative flexibility.

Graf Industries, headquartered in Nonantola (MO, Italy), is a multi-business company operating in sectors ranging from automation for fixtures to electrical systems management, software development, and alternative energy solutions. The PriXel project is an example of Graf Industries' commitment to push the boundaries of current technologies through the continuous innovation by Graf Inventa.

CONTRIBUTI ORALI

O1: IN SILICO ANALYSIS OF FIBROBLAST ACTIVATION PROTEIN: NEW INSIGHTS INTO PROTEIN ENDOPEPTIDASE ACTIVITY AND COVALENT INHIBITORS SELECTIVITY

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ABSTRACT

Fibroblast Activation Protein (FAP) is a serine protease belonging to the Prolyl Peptidase protein family. FAP has no crucial roles in physiological tissues while it is over and selectively expressed in tumors, where it is involved in angiogenesis and in remodeling the structure and composition of the extracellular matrix [1]. Although FAP presents a high sequence homology with dipeptidyl peptidase IV (DPP-IV), a common target for antidiabetic compounds, its peculiar endopeptidase activity can be exploited for the rational design of potent and selective inhibitors with theragnostic activity useful for tumor imaging. The (4-quinolinoyl)glycyl-2-cyanopyrrolidine, a pseudo-peptide compound characterized by a nitrile warhead, developed by Jansen et al., is one of the most known potent FAP covalent inhibitor [2]. As to date there are no experimental 3D structures of FAP protein in complex with covalent inhibitors available, their mechanism of action remains unclear. Through an in-depth *In-silico* analysis combining different computational techniques such as covalent docking and molecular dynamics we rationalized the known ligand structure-activity relationships and the observed FAP inhibitor selectivity (Figure 1). As such, the developed and validated computational workflow can guide the rational *De Novo* design and/or the optimization of known inhibitors structure to increase their residence time, a crucial parameter for theragnostic applications.

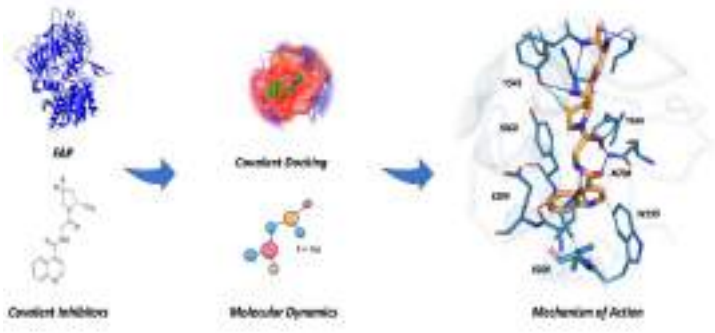

Figure. An In-Silico approaches combining covalent docking and molecular dynamics revealed new structural insights into ligand selectivity

REFERENCES

[1] E. J. Hamson, F. M. Keane, S. Tholen, O. Schilling, and M. D. Gorrell, "Understanding fibroblast activation protein (FAP): Substrates, activities, expression and targeting for cancer therapy," *Proteomics Clin Appl*, vol. 8, no. 5–6, pp. 454–463, Jun. 2014, doi: 10.1002/prca.201300095.

[2] K. Jansen et al., "Extended Structure–Activity Relationship and Pharmacokinetic Investigation of (4-Quinolinoyl)glycyl-2-cyanopyrrolidine Inhibitors of Fibroblast Activation Protein (FAP)," J Med Chem, vol. 57, no. 7, pp. 3053–3074, Apr. 2014, doi: 10.1021/jm500031w.

O2: COPPER(II) SALBEN COMPLEXES AS SUSTAINABLE CATALYSTS FOR C-N COUPLING

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ABSTRACT

Palladium-catalyzed coupling reactions has become a fundamental tool in synthesis. As of today, it is the second most used synthetic methodology in the pharmaceutical industry [1]. However, the increasing palladium price, its considerable carbon footprint, and high toxicity, has driven in the past decade the development of more eco-friendly and cost-effective alternatives. In this context, copper emerged as a very promising alternative. Herein, we present the copper(II) salben complexes (Fig. 1b, X = H) as highly efficient catalysts for the coupling of aryl iodides with a broad range of N-nucleophiles.
Copper(II) salben catalyst is derived from the H_2salben ligand (Fig. 1a, X = H) [2-6], a Schiff base with an N_2O_2 tetradentate system featuring only one carbon atom bridging the two iminic groups. This characteristic selectively leads to the formation of binuclear complexes, rather than mononuclear ones, with a distorted coordination geometry between tetrahedral and square planar around the metal centre [2-6]. Copper(II) salben is stable in air as a copper(II) species but is easily activated *in situ*, making it ideal for catalytic applications.
In particular in this contribution, we present the synthesis and characterization of a series of differently substituted sal(X)ben copper(II) complexes (Fig. 1b). We used a prototype C-N coupling reaction (Fig. 1c) to compare the catalytic performances of the different complexes. The best-performing catalyst demonstrated high reactivity and selectivity, affording the coupling product in high yields at low catalytic loadings and under relatively mild conditions. Lastly, the evaluation of the reaction scope highlighted the catalyst activity toward a broad range of aryl-iodide and N-nucleophiles.

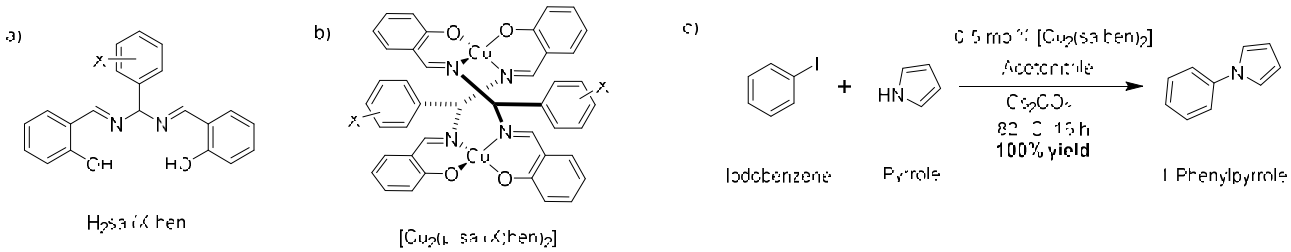

Figure 1: Molecular scheme of a) H_2sal(X)ben and b) [Cu_2(μ-sal(X)ben$_2$]; c) prototype catalytic reaction.

ACKNOWLEDGEMENTS
Dipartimento di Scienze Chimiche e Geologiche of the Università degli Studi di Modena e Reggio Emilia for the funding through the Fondo Dipartimentale per la Ricerca 2021, linea dottorato (FDR 2021).

REFERENCES
[1] D. G. Brown et al., *J. Med. Chem.*, **2015**, *59*, 10, 4443-4458
[2] A. Pasini et al., *J. Chem. Soc., Dalton Trans.*, **2000**, 3467–3472.
[3] B. Chiari et al., *J. Chem. Soc., Dalton Trans.* **2001**, 3611–3616.
[4] B. Chiari et al., *J. Chem. Soc., Dalton Trans.* **2002**, 4672–4677.
[5] L. Rigamonti et al., *Int. J. Mol. Sci.*, **2020**, *21*, 7882.
[6] L. Marchi et al., *Int. J. Mol. Sci.*, **2023**, *24*, 5808.

O3: ENGINEERED M13 PHAGES FOR ENHANCED ELECTROCHEMILUMINESCENT SIGNAL TRANSDUCTION IN POINT-OF-CARE BIOSENSORS

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ABSTRACT

Electrochemiluminescence (ECL) has become a key tool in bioanalytics, particularly for biomarker detection such as nucleic acids, proteins, cells, and viruses, thanks to its high signal-to-noise ratios. Traditional ECL biosensors typically use antibody sandwich assays that rely on capturing elements combined with transducer antibodies tagged with ECL-active dyes. Bacteriophages, with their ability to carry large amounts of photoactive molecules and display diverse targeting motifs on their capsids, offer a versatile platform for developing novel biosensors. This study introduces a phage-based ECL biosensor capable of rapid, whole-virus detection. Specifically, M13 bacteriophages were engineered to display a nanobody targeting the receptor binding domain (RBD) of the SARS-CoV-2 spike protein, fused to the minor coat protein pIII. The capsid of the modified $M13_{S1}$ virion was chemically conjugated with hundreds of ECL dyes, enhancing its detection capabilities by two orders of magnitude. The targeting efficiency of the conjugated phages was validated via flow cytometry, leveraging the intrinsic fluorescence of the ECL dyes, and in ECL assays, which revealed a substantial signal increase compared to antibody-based systems, achieving attomolar-level detection of SARS-CoV-2 virions in under an hour. This work demonstrates that phage-based ECL transducers provide significant advantages over antibodies, including increased sensitivity, reduced analysis time, and lower production costs. Additionally, the ease of use of the system and its portability can simplify SARS-CoV-2 detection by potentially removing the need for PCR amplification, making it accessible for non-specialist use.

Moreover, this approach could be extended to many other pathogen agents using M13 phages engineered to display proteins that selectively recognize the pathogen of interest.

REFERENCES

[1] Romano G, Insero G, Marrugat SN, Fusi F. (2022), Innovative light sources for phototherapy, Biomol Concepts. 13(1), 256-271

[2] Melissa E. K. Carter and others (2010), A Subtype of a Pseudomonas aeruginosa Cystic Fibrosis Epidemic Strain Exhibits Enhanced Virulence in a Murine Model of Acute Respiratory Infection, The Journal of Infectious Diseases, 202(6), 935–942

O4: SODIUM BICARBONATE: A SAFE SOLID CO_2 SURROGATE FOR MECHANOCHEMICAL CARBOXYLATION AND ^{13}C-LABELING

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ABSTRACT

In the realm of mechanochemistry the integration of gaseous reactants in solid-gas reactions has been recently emerging as a viable synthetic strategy.[1] However, technical challenges associated with handling and storing gases can result in safety hazards and economic drawbacks, limiting the wide application of potentially attractive methodologies.

Benign solid surrogates offer several benefits, including safe and simple reagent handling, eliminating the risks associated with hazardous gases.[2] Furthermore, solid compounds are ideal for ball milling, a technique that facilitates solvent-free reactions and often leads to faster reaction times.

Among the synthetic useful gases, the undeniable versatility of CO_2 as a C1 source makes it a cornerstone of modern synthetic strategies, both for fine and bulk chemicals.[3] Concerning carbon dioxide, the implementation of mechanochemical carboxylative reactions using a solid surrogate remains poorly investigated.

Figure 1. Mechanochemical activation of $NaHCO_3$

Herein, we describe the use of $NaHCO_3$ as an extremely cheap, safe, and easy to handle solid CO_2 surrogate for carboxylation reactions.[4] Industrially relevant chemicals such as cyclic carbamates and carbonates can be efficiently obtained from $NaHCO_3$ and the corresponding propargylamines and epoxides under mechanochemical conditions.

Notably, ^{13}C-Labeling of pharmaceutically active molecules such as Toloxatone and Linezolid precursors is achieved without gases or pressure, simplifying the process. Our novel carbon labeling method efficiently incorporates ^{13}C into bioactive compounds using minimal specialized equipment.

REFERENCES

[1] Bolm C.; Hernández J. G., Angew. Chem. Int. Ed., 2019, 58, 3285–3299.
[2] Turberg M.; Ardila-Fierro K. J.; Bolm C.; Hernández K. J., Angew. Chem. Int. Ed., 2018, 57, 10718–10722.
[3] Aresta M.; A. Dibenedetto A.;Angelini A., Chem. Rev., 2014, 114, 1709–1742.
[4] Mele F; Della Ca' et al., ChemRxiv, 2024; doi:10.26434/chemrxiv-2024-zm9fw

PRESENTAZIONI FLASH

F01: DESIGN AND SYNTHESIS OF SMALL MOLECULES TARGETING PRE-MIRNA21 TOWARD THE DEVELOPMENT OF RIBONUCLEASE TARGETING CHIMERAS (RIBOTACS) TO REGULATE THE ONCOGENIC MIRNA21

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ABSTRACT

RNA has emerged as a promising target for small-molecule drug discovery due to its ability to fold into complex secondary and tertiary structures that reveal accessible binding sites.[1] Among these, pre-miRNA-21, a non-coding RNA linked to various cancers and other diseases,[2] represents a validated therapeutic target of high interest. This project focuses on developing selective binders for pre-miRNA-21 to reduce miRNA-21 levels effectively. We began our screening with over 30 compounds using high-resolution native mass spectrometry (HR-MS), identifying top "hits" based on the affinity of our compounds for pre-miRNA-21 to inform structure-activity relationship (SAR) studies. These initial hits have led to a fragment-growth strategy producing derivatives with enhanced binding affinity to a pre-miRNA-21 construct. In parallel, we are employing RIBOTAC technology to engineer Ribonuclease Targeting Chimeras, using optimized ligands as "warheads." RIBOTACs are a novel class of heterobifunctional small molecules that comprise an RNA binder conjugated via a linker to another small molecule that recruits and activates RNase L. [Figure 1].[3] The formation of a ternary complex between the ROI, RIBOTAC, and RNase L leads to a proximity-induced degradation mechanism to achieve selectivity for the target RNA. So far, we have synthesized over five RIBOTACs. Upcoming studies will test the affinity, selectivity, and miRNA-21 inhibition of these warheads, applying biophysical and biochemical methods, such as NMR and DSF, using both recombinant enzyme assays and cell lysates.[4] Following these initial assessments, we plan to evaluate RIBOTAC efficacy in a series of targeted in-cell assays. This will enable us to characterize phenotypic outcomes and better understand the therapeutic potential of the RIBOTACs. Through this integrated approach, we aim to identify the optimal inhibitor and the most effective miRNA-21 degrader, advancing RNA-targeted therapeutic development.

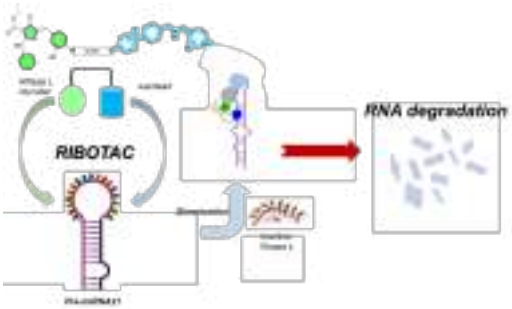

Figure 1: Mechanism of action of a RIBOTAC targeting pre-miRNA-21: binding, recruitment, and activation of RNase L, leading to RNA degradation and reduction of oncogenic miRNA-21.

REFERENCES

[1] A. Hargrove et al., *E. Chem Commun*, 2020, **56**, 14744-14756.
[2] M. D. Disney et al., *PNAS*, 2020, **117**, 33197–33203.
[3] M. D. Disney et al., *J. Am. Chem. Soc.*, 2021, **143**, 13044–13055.
[4] M. Duca et al., *J. Med. Chem.*, 2023, **66** (15), 10639-10657.

F02: STRUCTURE-ACTIVITY STUDIES OF A PNA-APTAMER FOR CARDIAC TROPONIN I USING ADVANCED SENSING TECHNIQUES

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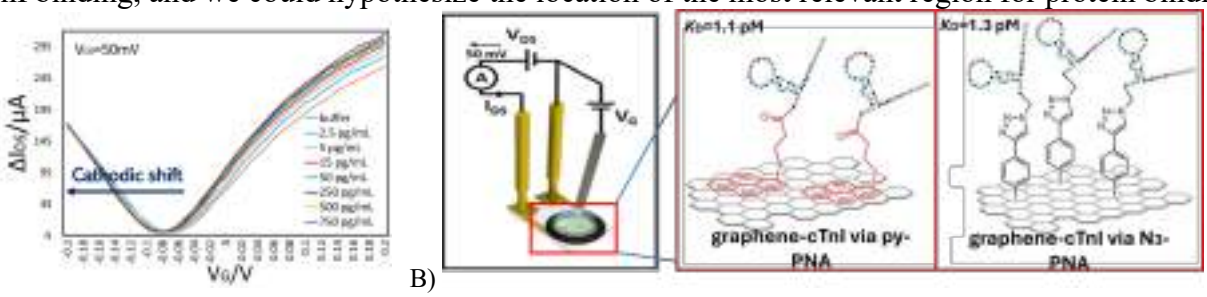
ABSTRACT

Peptide Nucleic Acids (PNAs) are synthetic mimics of DNA with a pseudopeptide backbone, and widely used to bind to complementary oligonucleotides. Being multifunctional molecules, PNAs can interact with a variety of biopolymers, including proteins; however, the interaction between PNAs and proteins remains largely unexplored. Since DNA and RNA aptamers are widely used for specific protein binding, we tested the use of PNAs in this field. PNA-aptamers might offer some advantages due to their enhanced biostability. A high-affinity PNA-aptamer for cardiac Troponin I (cTnI), an important biomarker for myocardial infarction, has been reported by our group [1]. This PNA was used integrated as bioreceptor on the surface of a graphene-based field effect transistor (gFET) where it showed picoMolar affinity for its target cTnI. Understanding the structure of this PNA-protein complex and the interactions involved will allow the design of other PNA-aptamers for different targets and could enable full comprehension of PNA-protein interactions. In this work we used Surface Plasmon Resonance (SPR) to measure and compare the dissociation constants (K_D) of various PNA-aptamers with cTnI for a better understanding of the possible binding sites between PNA and cTnI. We synthetized a series of segments and variants of the PNA aptamer and, to allow coupling with the sensor's surface, the PNA chains were modified either with a terminal pyrene (py-PNA), for non-covalent functionalization, or with a terminal azide (N_3-PNA), for covalent linkage through click chemistry (**Figure 1B**). We found comparable results for py-PNA or N_3-PNA with K_D values all in the picomolar range. We inferred that a stem-loop structure is not essential for cTnI binding, and we could hypothesize the location of the most relevant region for protein binding.



A) B)

Figure 1: A) ΔI_{DS}-V_G curves for py-PNA aptamer-based gFET titration of cTnI in 1x PBS, applied V_{DS}=50 mV. B) Scheme of the FET architecture and electrode connections used for electronic cTnI sensing (left), PNA modified graphene functionalized with py-PNA (center) or covalently by N3-PNA (right).

Using a gFET readout, we demonstrated the sensor's capability to bind cTnI under physiological relevant ionic strength (**Figure 1A**). Furthermore, PNA-based SPR sensors show improved stability in presence of DNase I with no loss of sensitivity or changes in the apparent K_D, compared to DNA-based SPR sensors. Initial studies of the PNA-aptamer conformation using Molecular Dynamics (MD) simulations will also be described.

REFERENCES

[1] T. Rodrigues, F. Curti, YR. Leroux et al., *Nano Today* 2023, 50, 101840.

F03: DYNAMIC HEADSPACE SAMPLING FOR VOLATILE PFAS FOLLOWED BY GC-MS AND GC×GC-MS

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ABSTRACT

Per- and polyfluoroalkyl substances (PFAS) represent a family of manufactured compounds which have been widely used in industry since the 50s. Chemically, they are composed of a carbon chain bonded to fluorine atoms, with different functional groups at the end of the chain. The persistence in the environment and potential impact on health of these substances make it crucial to establish reliable analytical methods for their detection. The purpose of this study is to evaluate the potential of thermal desorption tubes (a solvent-free, highly effective alternative to traditional methods) associated with gas chromatography and two-dimensional gas chromatography coupled with time-of-flight mass spectrometry to extract and identify (semi)volatile PFASs.
The performance of thermal desorption tubes was evaluated by testing various sorbents (graphitized carbon black and phenylphenylenoxide polymers) along with different extraction parameters (conditioning temperature and extraction volume). The objective was to assess recovery and selectivity in terms of PFAS extraction. The extraction processes were optimized simulating environmental samples, using a certificate soil and DI water, spiked with a mixture of PFAS standards (MW range 264-571 Da), including fluorotelomer alcohols (FTOH), acrylates (FTAc), and alkyl sulfonamide (N-MeFOSA, N-EtFOSA, N-MeFOSE, and N-EtFOSE) derivatives.
The most effective sorbent was poly(2,6-diphenylphenylene oxide) which is a type of porous polymer, even though using graphitized carbon adsorbent was also helpful for the extraction of specific compounds. GC×GC was used to identify other major molecules in environmental samples and TOFMS to analyze the individual PFASs, even those belonging to the same subfamily, showing its effectiveness in differentiating between them.
Conducting these primary tests was crucial in comprehending the behavior of PFAS compounds concerning their families both as standards and in actual samples. The thermal desorption tubes proved to be effective for extracting these compounds while minimizing the use of solvents. When combined with (GC×)GC-TOFMS, the method provides an alternative to traditional extraction methods.

F04: TARGETED METABOLOMICS FOR THE ANALYSIS OF *P*-CRESOL IN MOUSE BRAIN BY HPLC-ESI-MS/MS

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ABSTRACT

p-Cresol, an environmental contaminant and endogenous metabolite primarily derived from tyrosine conversion by intestinal microflora, is gaining increasing attention for its potential health impact. Once produced, the compound is converted into *p*-cresyl-glucuronide and *p*-cresyl-sulfate and excreted via organic anion transporters (OAT), which are also expressed in the brain, mediating efflux across the blood-brain barrier (BBB). While the impact of *p*-cresol and its metabolites as uremic toxins in chronic kidney disease (CKD) is well-known, affecting the central nervous, immune, and cardiovascular systems, their role in neurodegenerative and neurodevelopmental disorders is still under investigation. Elevated urinary levels of *p*-cresol and *p*-cresyl-sulfate have been found in autistic children with altered intestinal microbiota, suggesting a link to increased autism severity and gut dysfunction [1,2]. Moreover, *p*-cresol's effects on dopamine metabolism suggest possible roles in post-traumatic stress disorder (PTSD) and Parkinson's disease (PD) [3]. However, the evidence on the presence and concentration of *p*-cresol in the central nervous system (CNS) is virtually unknown, highlighting the need to develop an analytical method capable of quantifying this compound at very low concentrations.

To address this gap, we optimized and validated a new HPLC-ESI-MS/MS method for targeted metabolomics of *p*-cresol in brain areas. Using reversed-phase HPLC with gradient elution coupled with electrospray ionization-mass spectrometry (ESI-MS/MS) detection in multiple reaction monitoring (MRM) mode, we analyzed brain tissue from male and female C57BL/6 mice, revealing *p*-cresol distribution across seven brain regions. Additional measurements in the cortex of three mouse strains - CD1, C57BL/6 and the model of idiopathic autism BTBR +tf/J - showed that *p*-cresol levels were influenced by both sex and genotype. This effect was also observed in experiments on wild-type (WT) and CX3CR1 knockout (KO) mice: while sex and genotype affected *p*-cresol distribution in the prefrontal cortex, treatment with lipopolysaccharide (LPS) did not produce any significant changes in *p*-cresol levels. Additional targeted metabolomic analyses were performed to further explore potential correlations between this compound, neurotransmitters and their metabolites, particularly in dopaminergic and noradrenergic pathways. Preliminary analyses on human cortex samples also confirmed the presence of *p*-cresol, underscoring its potential relevance to brain health. Finally, molecular docking studies on OAT provided insights into potential BBB transport mechanisms for *p*-cresol and its derivatives. The determination of basal *p*-cresol levels in the brain lays the groundwork for studying its role in neurodevelopmental and neurodegenerative diseases. Future research will explore whether targeting transporters may interfere with its accumulation, offering new therapeutic strategies for autism, PTSD and PD.

REFERENCES

[1] Persico, A. M.; Napolioni, V., *Neurotoxicol. Teratol.* **2013**, *36*, 82–90. https://doi.org/10.1016/j.ntt.2012.09.002.
[2] Bermudez-Martin, P. et al., *Microbiome* **2021**, *9* (1), 157. https://doi.org/10.1186/s40168-021-01103-z.
[3] Laudani, S. et al., *Brain. Behav. Immun.* **2023**, *107*, 385–396. https://doi.org/10.1016/j.bbi.2022.11.004.
[4] Korytowska, N. et al., J. *Pharm. Biomed. Anal.* **2019**, *167*, 149–154. https://doi.org/10.1016/j.jpba.2019.01.041.

F05: DESIGNING G-QUADRUPLEX BINDERS FROM BENZO[D]IMIDAZO[2,1-B]THIAZOLE FRAMEWORKS: TOWARDS NOVEL ANTIPROLIFERATIVE AGENTS

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ABSTRACT

The identification of a diimidazopyrimidine scaffold[1] as an active structure for targeting G-quadruplex (G4) has led to the discovery of promising hit compounds (**Figure 1, a**).[2,3] In this context, many efforts have been done to optimize the activity and the selectivity of the analogues, diversifying the chemical space. In order to do so, we employed a scaffold-hopping approach, exploring alternative aromatic core structures to expand our compound series. Through application of a general synthetic scheme, a series of compounds bearing iminoguanidine or hydrazinoimidazoline side chains was synthetized and later underwent extensive evaluations to assess their G4-binding capabilities. Among the tested compounds, two emerged as promising candidates, bearing a benzo[d]imidazo[2,1-b]thiazole core (**Figure 1, H, I**). Based on these findings, we kept the scaffold while systematically modifying the side chains, also through saturation of the linking bond, improving mobility and chance of interactions with the phosphate backbone, generating new derivatives with distinct structural features. Our results provide insights into the structure-activity relationships of these scaffolds, demonstrating the potential of benzo[d]imidazo[2,1-b]thiazole derivatives as promising G4 binders for further development in cancer therapeutics. This iterative process of scaffold modification and biophysical assessments will contribute to the development of novel antiproliferative agents targeting G4 DNA, whose activity is now being studied.

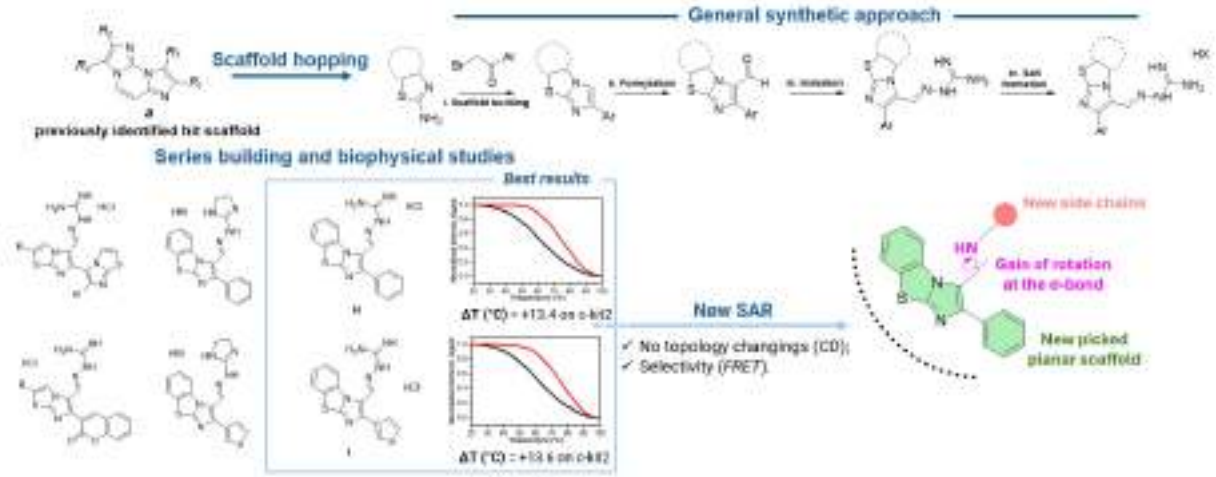

Figure 1

REFERENCES

[1] Amato, J.; Morigi, R.; Pagano, B.; Pagano, A.; Ohnmacht, S.; De Magis, A.; Tiang, Y. P.; Capranico, G.; Locatelli, A.; Graziadio, A.; Leoni, A.; Rambaldi, M.; Novellino, E.; Neidle, S.; Randazzo, A.* J Med Chem 2016, 59 (12), 5706–5720;
[2] De Magis, A.; Manzo, S. G.; Russo, M.; Marinello, J.; Morigi, R.; Sordet, O.; Capranico, G.* *Proc Natl Acad Sci U S A* 2019,*116* (3), 816–825;
[3] Marzano, S.; Miglietta, G.; Morigi, R.*; Marinello, J.; Arleo, A.; Procacci, M.; Locatelli, A.; Leoni, A.; Pagano, B.; Randazzo, A.; Amato, J.*; Capranico, G.* J Med Chem 2022, 65 (18), 12055–12067.

F06: LIPIDOMIC ANALYSIS IDENTIFIES GLYCOSPHINGOLIPID METABOLISM AS A TARGET FOR OVERCOMING OSIMERTINIB RESISTANCE IN NON-SMALL CELL LUNG CANCER

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ABSTRACT

Increased ceramide glycosylation has been recognized as a key trait in various clones resistant to osimertinib (OSI), presenting a novel target to combat metabolic reprogramming associated with tumor resistance.[1]
Using the OSI-sensitive NSCLC cell line PC9, we assessed the changes in lipid metabolism induced by the co-treatment with osimertinib (OSI) and a glucosylceramide synthase (GCS) inhibitor, either D-threo-1-phenyl-2-decanoylamino-3-morpholino-1-propanol (PDMP) or venglustat, at various concentrations.
An untargeted lipidomic analysis on PC9 cell extracts was conducted by ultra-high-performance liquid chromatography coupled with high resolution mass spectrometry.
A dose-dependent increase in glycosylceramide signal intensities was observed in relation to the concentration of the GCS inhibitor, which correlated with the suppression of OSI-resistant clone formation in OSI-sensitive cell lines treated with OSI over an extended period. This suggests that combining a GCS inhibitor with an EGFR-targeting tyrosine kinase inhibitor could be a promising strategy in postponing the onset of drug resistance.

REFERENCES

[1] La Monica, S., Vacondio, F., Eltayeb, K. et al. Sci Rep, **2024**; 14, 6491.

F07: ELEVATING METABOLOMIC PROFILING: INTEGRATING ADVANCED CHROMATOGRAPHY AND HIGH-RESOLUTION MASS SPECTROMETRY FOR COMPRENHENSIVE BIOMARKER DISCOVERY IN CLINICAL STUDIES

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ABSTRACT

Metabolomics, a rapidly evolving field, provides profound insights into the quantitative and qualitative assessment of metabolites across various domains, including medicine, environment, nutrition, and agriculture. This scientific discipline facilitates global identification of metabolites, offering crucial insights into metabolic profiles and biomarker discovery. Metabolomics analysis is pivotal in comprehending biological processes and human diseases, demanding advanced analytical methodologies to unravel the complexity of the metabolome. Integration of semi-targeted methodologies, such as the use of internal standards (ISTDs), with untargeted approaches is crucial. This work combines parallel liquid chromatography with high-resolution mass spectrometry (HRMS) as a promising approach to cover metabolites over a wide polarity range in clinical studies such as for detection of leaky gut [1].
The diversity of human metabolites, characterised by a wide range of polarities, also requires the implementation of highly sophisticated liquid chromatography systems. In this regard, the use of parallel chromatography, equipped with two binary pumps, two injectors and two column compartments, is crucial. This approach allows the simultaneous application of two complementary separation techniques: reversed phase chromatography (RP) and hydrophilic interaction chromatography (HILIC). This optimised combination, together with the use of high-resolution mass spectrometry (HRMS), allows maximum metabolite coverage and accurate detection of metabolites with different chemical characteristics.
In this work, with the aid of parallel chromatography and the implementation of high-resolution mass spectrometry (HRMS), it was possible to identify a wide range of metabolites in a broad polarity range in patients affected by resistant treatment depression [2]. Moreover, metabolites of different classes were identified by means of semi-targeted approaches through the use of internal standards (ISTDs) or non-targeted approaches through the comparison of experimental data with data in the Human Metabolome Database (HMDB). In conclusion, the integration of semi-targeted methodologies, untargeted approaches and the adoption of advanced liquid chromatography systems represent an effective strategy to address the complexity of the human metabolome, enabling a better understanding of biological processes and the identification of clinically relevant biomarkers.

REFERENCES

[1] Camilleri M: Leaky gut: mechanisms, measurement, and clinical implications in humans. Gut 2019; 68:1516
[2] Kelly JR, Kennedy PJ, Cryan JF, et al: Breaking down the barriers: the gut microbiome, intestinal permeability and stress-related psychiatric disorders. Front Cell Neuroscience 2015; 9:392

F08: ONE-STEP TECHNIQUE FOR THE SELF-ASSEMBLY OF FULLY NATURAL LACTOFERRIN NANOMEDICINES FOR GENE DELIVERY

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ABSTRACT

Self-assembling nanomaterials hold immense promise in the field of nanomedicine and drug delivery, enabling efficient and scalable production of drug delivery systems with enhanced precision and reproducibility. By reducing the need for excipients, stabilizers, large amounts of toxic organic solvents, and high-energy techniques, they simplify production and enhance industrial appeal. In this project, we focused on lactoferrin (LF), a natural multifunctional glycoprotein exhibiting highly favorable properties such as biodegradability, biocompatibility, and targeting ability along with a unique self-assembling behavior triggered by heat-induced controlled denaturation [1]. Furthermore, its use as a natural biomaterial for NMed self-assembly can further enhance this attractiveness due to its inherent biodegradability and biocompatibility, which reduce the likelihood of side effects and adverse reactions following administration. These features of LF have allowed us to develop highly homogenous single-component and fully natural non-loaded nanomedicines (NMeds) through a one-step, rapid, reproducible, and sustainable process. Optimized LF NPs exhibited a particle size around 60-70 nm, a polydispersity index (PdI) lower than 0.2, positive surface charge (Z-potential of approximately +30 mV), and remarkable storage stability without the need for stabilizers or additives. By exploiting the cationic nature of LF, we also created LF NMeds designed for gene therapy and specifically complexing, stabilizing, and delivering small interfering RNA (siRNA), a highly selective and potent RNA-based therapeutic which alone faces challenges such as enzymatic degradation and low cellular uptake [2]. LF-siRNA NMeds exhibited unchanged physicochemical and stability properties compared to non-loaded LF NMeds, along with a high siRNA complexation efficiency and protection from RNase degrading enzymes. *In vitro* studies are now being performed to assess both the biosafety and efficacy of LF-siRNA NMeds, particularly focusing on the transfection efficiency and anti-cancer effect in different cancer cell models (glioblastoma, pancreatic carcinoma, metastatic melanoma). To the best of our knowledge, this work represents the first application of LF self-assembling properties for siRNA delivery, offering a rapid, reproducible, sustainable, and scalable strategy to produce effective gene delivery nanosystems.

REFERENCES

[1] Elzoghby, A.O.; Abdelmoneem, M.A.; Hassanin, I.A.; Abd Elwakil, M.M.; Elnaggar, M.A.; Mokhtar, S.; Fang, J.-Y.; Elkhodairy, K.A. Lactoferrin, a Multi-Functional Glycoprotein: Active Therapeutic, Drug Nanocarrier & Targeting Ligand. *Biomaterials* **2020**, *263*, 120355, doi:10.1016/j.biomaterials.2020.120355.

[2] Hu, B.; Zhong, L.; Weng, Y.; Peng, L.; Huang, Y.; Zhao, Y.; Liang, X.-J. Therapeutic siRNA: State of the Art. *Signal Transduct. Target. Ther.* **2020**, *5*, 101, doi:10.1038/s41392-020-0207-x.

F09: ENANTIOSELECTIVE THREE-COMPONENT REACTION OF SULFOXONIUM YLIDE, THIOLS AND ALDEHYDES.

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ABSTRACT

Enantioselective three-component reactions (3CRs) have demonstrated broad applicability in organic chemistry since they represent a rapid and useful way for the synthesis of complex molecules. Among these, onium-ylide-mediated 3CRs, involving a metal carbene, a nucleophile, and an electrophile, have been reported by different groups.[1-4] Hu end co-workers used this approach for the enantioselective synthesis of diverse scaffolds, including α-mercapto-β-amino esters (Figure 1a).[3] These reactions typically require diazo compounds as precursors of the carbene species, and are catalyzed by a synergistic combination of a metal and a chiral phosphoric acid (CPA). Furthermore, diazo compounds have significant limitations such as thermal instability, difficult preparation, release of N_2 gas and toxicity. To overcome these issues, especially in large-scale preparations, sulfur ylides have emerged as a safer and more stable alternative to diazo compounds. We described the first example of an asymmetric organocatalytic 3CR involving sulfoxonium ylides (Figure 1b). Additionally, unlike diazo compounds, this platform also enables the formation of tertiary stereocenters, further expanding the range of accessible molecular architectures. Despite some challenges that arise from potential side reactions, such as the S-H insertion reported by Burtoloso,[5-6] and the high reactivity of monosubstituted sulfoxonium ylides, this transformation provides access to a scaffold that is otherwise challenging to obtain.

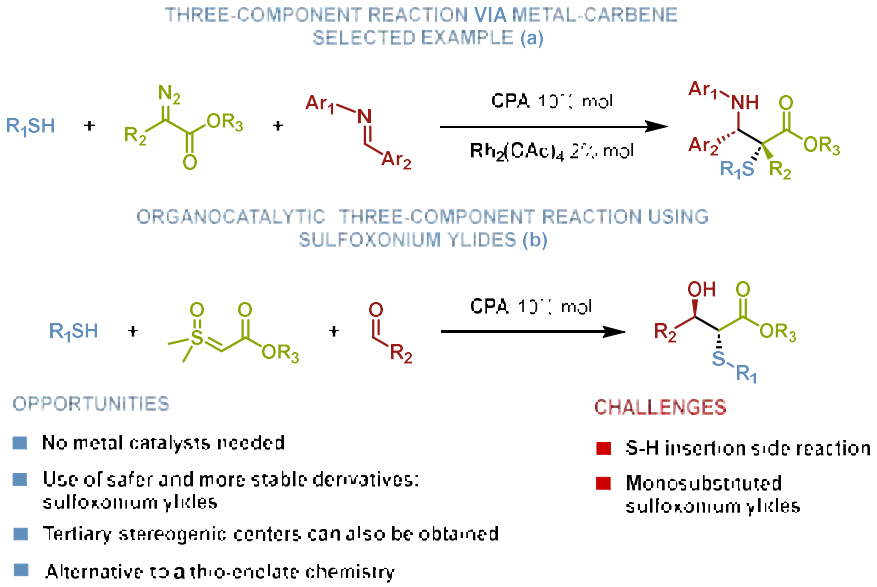

Figure 1: Comparison between enantioselective 3CRs mediated by diazo compounds (a) and sulfoxonium ylides (b).

REFERENCES

[1] C. Zhou, J. Wang, J. Wei, Z. Xu, Z. Guo, K. Low, C. Che, Angew. Chem. Int. Ed. 2012, 51, 11376.
[2] B. Alcaide, P. Almendros, C. Aragoncillo, R. Callejo, M. Ruiz, M. Torres, Eur. J. Org. Chem. 2012, 2359.
[3] G. Xiao, C. Ma, D.Xing, W. Hu, Org. Lett. 2016, 18, 6086.
[4] L. Ren, X. Lian, L. Gong, Chem. Eur. J. 2013, 19, 3315.
[5] R. M. P. Dias, A. C. B. Burtoloso, Org. Lett. 2016, 18, 3034.
[6] P. B. Momo, A. N. Leveille, E. H. E. Farrar, M. N. Grayson, A. E. Mattson, A. C. B. Burtoloso, Angew. Chem. Int. Ed. 2020, 59, 15554.

F10: TEMPLATE SYNTHESIS OF IMINOPHOSPHINE COPPER(I) COMPLEXES

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ABSTRACT

Copper(I) complexes find application in a wide variety of fields, ranging from medicine to catalysis and material science [1]. Soft ligands, such as P,N ligands, are able to stabilize copper in the oxidation state +1. Few Cu(I) complexes with iminophosphine ligands are reported in the literature [2], even though this class of ligands has been used extensively for the synthesis of complexes with gold [3] and palladium [4]. The iminophosphine derived from 2-(diphenylphosphino)benzaldehyde and benzylamine was chosen as prototype ligand for a panel of Cu(I) complexes. To overcome problems in the isolation of the ligand, related to solubility in most organic solvents and instability on silica, we exploited a template approach, obtaining directly the metal complexes. The Cu(I) precursor was reacted with the aldehyde and the amine in an acetonitrile/chloroform mixture. Such synthetic strategy allowed to isolate three different complexes by varying the aldehyde:Cu(I):amine ratio (1:1:1 and 2:1:2) and the anion (iodide or nitrate) (Fig. 1). We enlarged the panel of compounds, by introducing different substituents in the para-position of the aromatic ring: other six complexes were prepared by using 4-methylbenzylamine and 4-fluorobenzylamine. All these novel Cu(I) complexes were synthesized in a straightforward manner under dinitrogen atmosphere and without the need for dry conditions. They are all air and moisture stable in the solid state and no oxidation of Cu(I) was observed in solution. Furthermore, to elucidate the reaction mechanism, the Cu(I)-aldehyde intermediate complexes were isolated and characterized. The approach described herein for the preparation of novel Cu(I) complexes can be exploited to prepare systems with different pending groups, depending on the amine precursor. In view of a future application as antitumor metallodrug, the design and the synthesis of hydrophilic iminophosphine-Cu(I) complexes are currently ongoing.

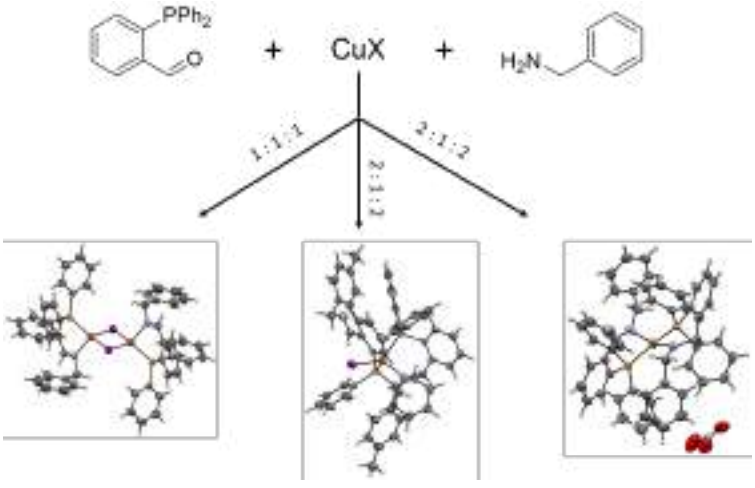

Figure 1. Schematic representation of the template synthesis of the Cu(I) complexes (X = I, NO_3).

REFERENCES

[1] J. Beaudelot et al., *Chemical Reviews,* **2022**, 122, 16365−16609.
[2] J. Süß et al., *Molbank*, **2024**, 2024, M1808.
[3] T. Traut-Johnstone et al., *Journal of Inorganic Biochemistry*, 145, **2015**, 108–120.
[4] J. Isai Ortega-Gaxiola, et al., *Inorganica Chimica Acta,* 504, **2020**, 119460.

POSTER

P001: PROMOTING A SUSTAINABLE MEDICINAL CHEMISTRY APPROACH WITH THE COST ACTION CA21111 - *ONE HEALTH DRUGS AGAINST PARASITIC VECTOR BORNE DISEASES IN EUROPE AND BEYOND.*

Daniele Aiello[a], Anabela Cordeiro-da-Silva[b], Lorenzo Tagliazucchi[a], Giulia Saporito[a], Giulia Malpezzi[a], COST Action CA2111 Members, Maria Paola Costi[a]

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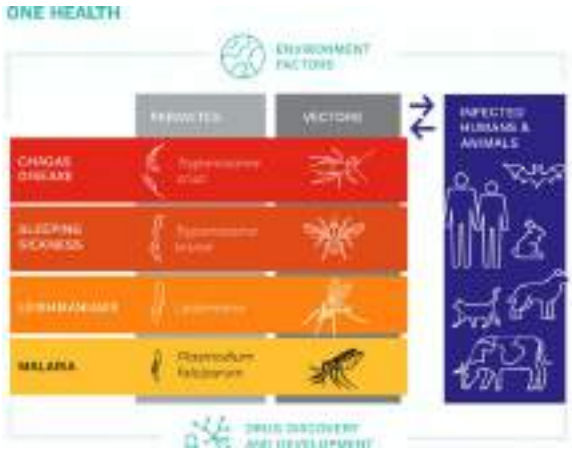
ABSTRACT

The recent COVID19 pandemic infection has undisclosed long-standing issues in the translation of drugs from animals to humans or vice-versa. Nearly 75% of emerging human infections worldwide originated from animals; existing drugs for human and animal (H&A) vector-borne diseases (VBD) are scarce, with limited efficacy, toxicity, and finite resources. Emerging environmental problems in pharmaceutical use/manufacturing increase attention in the field. The two drug pipelines are developed independently. Hence, cooperation is needed among different expertise to define how it is possible to develop new drugs in a more sustainable approach [1]. OneHealth*drugs* (OHD) COST Action, aims at coordinating the discovery of drugs halting H&A VBD keeping with the principles of optimal profile for both organisms, increasing the quality and delivery technologies [2]. OneHealth*drugs* is constituted by over 300 researchers, medicinal chemists, parasitologists, ecotoxicologists physicians, veterinarian and other personnel. It is the ideal platform aiming at the integration and generation of synergies among drug R&D experts from the chemical/ biological/human/veterinary and earth science (ecotoxicology) within academies, SMEs, industries, governments. The platform encompasses pre-clinical drug discovery, animal studies, and drug delivery. Strategies such as bioinformatics, advanced omics technologies, nanotechnology will be enhanced [2]. OneHealth*drugs* in two years of intensive activity is impacting in Europe, USA, reaching disease-endemic countries. The Action is providing a compounds database and will deliver a white chart about the innovative approach for the discovery of new drugs for H&A infections, more selective and environmentally safer. Expected benefits include a change of mentality in the drugs discovery and preclinical phases, in the transfer of academia-industry and Northern-Southern world knowledge [3]. Conferences, training schools, and STSMs are monthly executed, as well as novel communication technologies to disseminate the Action results to a broad audience including scientists, stakeholders, and citizens. Young researchers will be trained on advanced techniques. More information is available at https://www.onehealthdrugs.com



REFERENCES

[1] Lima CM, Uliassi E, Thoré ESJ, Bertram MG, Cardoso L, Cordeiro da Silva A, Costi MP, de Koning HP. Environmental impacts of drugs against parasitic vector-borne diseases and the need to integrate sustainability into their development and use. Open Res Eur. 2024 Nov 4;4:207. doi: 10.12688/openreseurope.18008.2. [2] https://www.cost.eu/actions/CA21111/ [3] Maria Paola Costi and Anabela Cordeiro da Silva. One Health and Vector-Borne Parasitic Diseases Virtual Special Issue. *ACS Infectious Diseases* DOI: 10.1021/acsinfecdis.4c00778

P002: RECYCLABLE AND SUSTAINABLE AZOLIUM-BASED ORGANOCATALYSTS IMMOBILIZED ON BAMBOO FOR MEDIATING C-O BOND FORMATION REACTIONS

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ABSTRACT

This study introduces innovative heterogeneous catalysts derived from triazolium and imidazolium compounds for facilitating C-O bond formation reactions. These homogeneous organocatalysts were successfully immobilized on pre-treated bamboo, chosen for its natural porosity, using different linker molecules (Figure 1).

Driven by the growing emphasis on eco-friendly methodologies in chemical synthesis, research has shifted towards identifying sustainable inert supports for molecular catalyst immobilization. Natural porous materials, such as bamboo, contribute to the overall sustainability of these processes.[1] Three-dimensional lignocellulosic materials, such as bamboo, represent a new frontier for microfluidic devices due to the ease of chemical functionalization of lignin and cellulose and their ability to immobilize catalysts. Unlike wood, which has limitations related to the tortuosity of its fibers, bamboo provides a straight and parallel vascular structure, making it ideal for sustainable microfluidic biosystems. Its mechanical, chemical, and thermal properties make bamboo an exceptionally efficient material for fluid transport.[2]

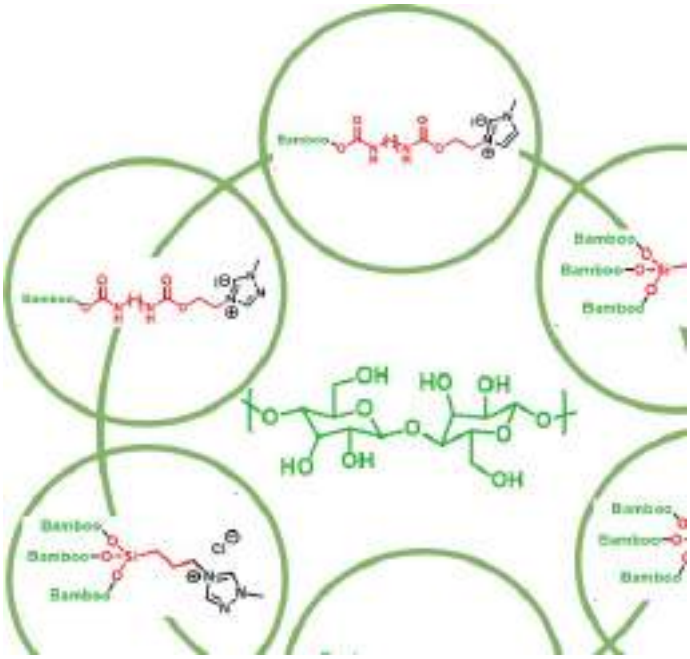

Figure 1. Heterogeneous organocatalysts immobilized onto bamboo with different linkers.

Specifically, the anchoring of 1-methylimidazole and 1-methyl-1,2,4-triazole onto bamboo was explored using silane and isocyanate chemistry to create linkages of varying lengths and polarities. Initial experiments focused on the synthesis of cyclic carbonates from epoxides and CO_2 using these bamboo-supported organocatalysts. Ongoing investigations aim to optimize their performance in both batch and continuous flow systems.

REFERENCES

[1] B. G. Palma, et al, Catalysis Today 381 (**2021**), 280-287
[2] G. Pandoli, O., et al, ACS Sustain. Chem. Eng. (**2019**), 7 (3), 3267–3273.

P003: EXPANDING THE SCOPE OF A NEW BIO-ORTHOGONAL TEMPLATED REACTION

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ABSTRACT

The desire to explore biomolecules and biological processes within their natural contexts has driven the development of reactions that are compatible with such environments. This pursuit presents a substantial challenge owing to the complexity of cellular systems. Reactions capable of proceeding within a biological system without disrupting native biological processes are termed "bioorthogonal reactions". Components involved must exhibit rapid and selective reactivity in water under phisiological conditions, in contexts of high molecular crowding.
Despite the remarkable advancements in bioorthogonal chemistries, so far very few ligation reactions have proven to be efficient at cellular level. Within current methodologies, challenges related to interference amidst the numerous functionalities present in vivo, and the requirement to remain non-toxic to the biological system, persists.
Our aim is to improve a recently discovered bio-orthogonal templated reaction which requires "proximiy" as sole trigger and expand his reactivity, ultimately extending its applicability to cellular studies.[1,2] The chosen reaction involves the ligation between 2,5-dioxopentanyl (DOP) moiety and an alpha nucleophile, resulting in the formation of piridazinium or pyrrole linkage (Fig.1). This reaction, which has been successfully tested in cell lysate, has demonstrated its ability to proceed exclusively under the guidance of a template, such as (peptide) nucleic acids or coiled-coil system formation, with high specificity and without off-target reactivity.
Here, we will present preliminar results regarding the synthesis of various alpha nucleophiles building blocks and preliminary ligation experiments performed on peptide nucleic acids (PNAs) models.

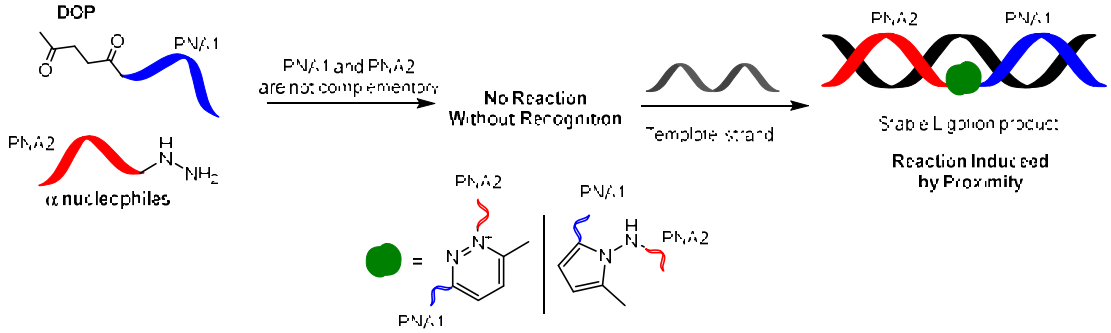

Figure 1. Templated Bio-Orthogonal Ligation

REFERENCES

[1] A. Manicardi, E. Cadoni, A. Madder, Communications Chemistry 2021, 4 (1), 146.
[2] A. Manicardi, A. Theppawong, M. Van Troys, A. Madder, Organic Letters 2023, 25 (36), 6618 – 6622.

P004: NANOPARTICLE ENCAPSULATION OF HINOKITIOL: APPROACHES IN FORMULATION AND *IN VITRO* PERFORMANCE

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ABSTRACT

Nanomedicine has emerged as one of the leading players for the treatment of orphan diseases [1-3]. One such disease is hemochromatosis (HC) which is a genetic disease characterized by an excess accumulation of iron in the blood and organs [4-5]. Combining nanomedicine with iron chelators is a promising way to treat this disease [6]. Primarily nanomedicines can protect the chelator, and improve its biodisponibility. Moreover, Nanomedicines offer the advantage of targeting, where a ligand can be added to the formulation to increase the accumulation in the liver or also in the central nervous system. In this project we optimized the formulation parameters to load Hinokitiol (HK) into four different types of biocompatible and biodegradable nanoparticles (NPs). i.e. polymeric NP, solid lipid nanoparticles (nanostructured lipid carriers, NLC), liposomes (neutral and cationic) and fully cholesterol (Chol) NPs. The physical formulation parameters were optimized, but the volatility of the drug molecule led to numerous difficulties in its encapsulation and quantification. Taking all of these into account, all the formulations resulted in nanoparticles that were approximately 100-300 nm with a good homogeneity represented by a PDI < 0.25. After the quantification of the loaded drug, we came to the conclusion that Chol NPs, NLC and polymeric NPs were the best to use for further *in vitro* and *in vivo* testing, thanks to a loading efficiency of almost 30% for Chol NPs and NLC, and almost 20% for polymeric NPs. Cell viability studies showed that at the standard efficient dose of 100 µM of HK [7], equivalent up to 300 µg/mL of NPs depending on the formulation, it was possible to treat HC model cell lines (J77A) with no observable toxicity. Interestingly, kinetics studies revealed that NPs loaded with HK were more efficient in lowering intracellular Iron levels compared to the free drug. These NPs at nontoxic doses are now being assessed *in vitro* and *ex vivo* for uptake and their therapeutic effect on HC patients' primary macrophage cultures. The success of these NPs are a breakthrough technology that could lead to an efficient, nontoxic, and improved treatment for diseases related to a systemic iron overload such as HC.

REFERENCES

[1] https://doi.org/10.1021/acsmaterialsau.3c00073
[2] https://doi.org/10.1038/s41578-023-00552-2
[3] https://doi.org/10.3390/pharmaceutics15030774
[4] https://doi.org/10.2174/0115734137243766230919062151
[5] https://doi.org/10.47750/pnr.2022.13.S10.645
[6] https://doi.org/10.1186/s13045-023-01460-2
[7] https://doi.org/10.1073/pnas.2121400119

P005: CLEAN PRODUCTION OF BENZYL BENZOATE USING CONVENTIONAL HEATING OR MICROWAVES-ASSISTED METHODS VIA BIOCATALYTIC APPROACH

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ABSTRACT

The increasing incidence of scabies worldwide and in Europe was recognized by the World Health Organization (WHO) as a significant public health problem that affects 130 to 300 million people annually[1]. In this context, benzyl benzoate (BB) is recommended as an efficacy and low-cost treatment concerning other scab therapies[2]. Additionally, recent studies suggested that benzyl esters, including BB, showed an activity-targeted drug against Covid-19 virus[3].
In this work, we described an efficient and sustainable process based on the exploitation of Lipozyme 435 lipase as green catalysts in a solventless system to afford the respective ester of methyl benzoate (MB) and benzyl alcohol (BA) with conventional heating or microwave-assisted[4]. Nowadays, it is widely known that biocatalysis has become an excellent alternative for the design of products with low environmental impact, as it follows several principles of green chemistry[5]. Hence, ecological factors, especially potential environmental impacts, are increasingly crucial for developing and implementing new or improved processes.
Herein, the BB was obtained with an alcohol-to-methyl ester molar ratio of 1:6, a temperature of 73 °C, and enzyme loading of 10% and 16% (w/w), for conventional heating and microwave-assisted, respectively. Under these specified experimental conditions, yields greater than 90% in 24 h and 82% in 7 h were obtained. Moreover, reuse studies of the biocatalyst were conducted. The results showed a good reusability of the commercial enzyme; indeed, the ester production remains stable for up to 4 use cycles. Finally, the product was analyzed via gas chromatography and proton NMR, and a high purity can be obtained by simple distillation.
Considering everything, the proposed clean production of BB can be considered a biosynthetic pathway where chemical innovation simultaneously achieves environmental and economic targets.

REFERENCES

[1] Lajarin-Reinares, M., Martinez-Esteve, E., Pena-Rodríguez, E., Cañellas-Santos, M., Bulut, S., Karabelas, K., Clauss, A., Nieto, C., Mallandrich, M., Fernandez-Campos, F., 2022. The efficacy and biopharmaceutical properties of a fixed-dose combination of disulfiram and benzyl benzoate. Int. J. Mol. Sci. 23, 10969.
[2] Heukelbach, J., Feldmeier, H., 2006. Scabies. Lancet 367, 1767–1774.
[3] Aydın, A.D., Altınel, F., Erdoğmuş, H., Son, Ç.D., 2021. Allergen fragrance molecules: a potential relief for COVID-19. BMC Complement Med. Ther. 21, 1–14.
[4] Aprile, S.; Venturi, V.; Presini, F.; Mustafa, A.; Sadek, M. S.; Inayat, A.; Remonatto, D.; Giovannini, P. P.; Lerin, L. A. Techno-Economic Assessment of Benzyl Benzoate Clean Production Using Conventional Heating or Microwaves. *Sustainable Chemistry and Pharmacy* **2023**, *36*, 101257.
[5] Anastas, P., Eghbali, N., 2009. Green chemistry: principles and practice. Chem. Soc. Rev. 39, 301–312.

P006: IN-SITU ELECTROCHEMICAL GENERATION OF INITIATOR FOR IONIC POLYMERIZATION OF DIENE AND VINYLARENE MONOMERS

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ABSTRACT

Lithium-based compounds are currently the most widely used initiators for traditional polymerization reactions, especially in industrial applications. However, their use poses environmental and economic challenges due to the hazardous nature, high reactivity, and substantial costs of lithium compounds[1]. In contrast, the electrochemical generation of initiators for living ionic polymerization offers a promising alternative. This method is safer, more cost-effective, and environmentally friendly as it avoids the need for lithium-based initiators. Additionally, the electrochemical approach allows for precise control over initiator generation, potentially enhancing the polymerization efficiency and product quality.

Our studies investigate the uses of α-olefins or polycyclic aromatic hydrocarbons (PAHs) such as anthracene, naphthalene, and phenanthrene as initiators[2]. The experimental investigation involves the development of an electrochemical and spectroelectrochemical setup on a laboratory scale. The initiators are electrochemically reduced by applying a constant reduction potential by amperometric analysis, leading to the generation of a reactive intermediate. This intermediate may be capable of initiating the polymerization process in the presence of specific monomers, such as styrene or butadiene. Our work can therefore provide a viable alternative to processes initiated using lithium-based compounds.

REFERENCES

[1] Xia, R.; Overa, S.; Jiao, F. Emerging Electrochemical Processes to Decarbonize the Chemical Industry. *JACS Au* **2022**, *2* (5), 1054–1070. https://doi.org/10.1021/jacsau.2c00138.

[2] Szwarc, M.; Levy, M.; Milkovich, R. POLYMERIZATION INITIATED BY ELECTRON TRANSFER TO MONOMER. A NEW METHOD OF FORMATION OF BLOCK POLYMERS [1]. *J. Am. Chem. Soc.* **1956**, *78* (11), 2656–2657. https://doi.org/10.1021/ja01592a101.

P007: DEVELOPMENT OF NEW CERAMIC BODIES USING INDUSTRIAL RECYCLED MATERIALS

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ABSTRACT

The ceramics industry is a "hard to abate" industrial sector characterised by high energy consumption and significant CO_2 emissions, which are particularly difficult to mitigate. The production of ceramics, especially porcelain stoneware, involves intensive energy use in the drying, firing and cooling stages, with more than 50% of the energy consumed concentrated in the firing stage, where temperatures of over 1200 °C are reached[1]. The high temperatures required to sinter the tiles and achieve the strength and low porosity characteristics typical of porcelain stoneware are currently mainly achieved using fossil fuels, which are difficult to replace with renewable energy sources. However, to meet the growing need for environmental sustainability, the ceramics industry is exploring new solutions to reduce the environmental impact and consumption of natural resources. One of the approaches is the integration of waste and by-products into ceramic bodies, transforming them from potentially polluting waste into resources for the production process[2]. The use of waste materials offers a double advantage: on the one hand, it reduces the consumption of virgin raw materials, thus conserving increasingly limited and expensive natural resources; on the other hand, it contributes to reducing energy costs thanks to the possibility of lowering firing temperatures. Waste materials act as additives or fluxes, facilitating sintering and allowing lower firing temperatures. This results in energy savings and reduced CO_2 emissions, improving the efficiency and sustainability of the production process. For example, the integration of recycled glass, in variable percentages between 10 and 15%, has demonstrated the ability to reduce firing temperatures by up to 100°C. This reduction in temperature results in a 3–7.5% decrease in energy costs and a reduction in CO_2 emissions of up to 19%, representing a sustainable and competitive solution for the ceramics sector[1].The aim of this research project is to study and optimize the use of waste materials from different sectors, such as ceramic powders, demolition waste and recycled glass, in porcelain stoneware bodies. Waste management and recycling are key to solving the landfill problem, a major global environmental challenge, and contribute to a circular economy model. This research will analyse different types of waste to determine their composition and the characteristics of the final product. The analysis of the firing behaviour of the different ceramic bodies will be carried out through laboratory tests, including measurement of linear shrinkage, water absorption and mechanical properties such as flexural strength, and studies with mineralogical and microstructural tests, with attention to the composition of crystalline phases and the distribution of recycled components. This approach aims to develop new ceramic bodies with reduced environmental impact by integrating waste that would otherwise be difficult to dispose of. Such integration also offers significant benefits to the manufacturing sector, saving on raw material purchase costs and energy costs, while responding to European regulatory pressures to reduce greenhouse gas emissions. The project therefore represents an opportunity for the ceramics industry to actively contribute to sustainability, maintain international competitiveness and promote an innovative, circular production model.

REFERENCES

[1] Dylan D. Furszyfer Del Rio et al., "Decarbonizing the ceramics industry: A systematic and critical review of policy options, developments and sociotechnical systems", Renewable and Sustainable Energy Reviews, Volume 157, 2022, 112081.
[2] Chiara Zanelli et al., "Waste recycling in ceramic tiles: a technological outlook, Resources, Conservation and Recycling", Volume 168, 2021, 105289.

P008:FISH-BASED FUNCTIONAL FOOD ENRICHMENT BY FEED FORMULATION: A METABOLOMIC AND BIOACCESSIBILITY STUDY

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ABSTRACT

The growing demand for healthy diet and functional foods has driven an increase in fish consumption, valued for its nutritional content rich in proteins, beneficial lipids, and micronutrients. This trend will continue with the rise in the global population, which is expected to exceed 9 billion by 2050, and the resulting increase in food demand. As a result, the production of fish products is projected to grow to 204.4 million tons by 2030, with global annual fish consumption estimated at 14.5%. Aquaculture production will increase from 82.1 to 108.5 million tons (+32.2%) [1], with species like salmon, trout, sea bream, bass, and carp seeing higher consumption [2]. Fish has beneficial effects on human health reducing the risk of chronic and inflammatory diseases. For this reason, fish products can be fortified to further enhance the nutrients already present, thereby improving their nutritional value. These functional foods contain essential ω-3 fatty acids, carotenoids, chitosan, taurine, choline, vitamins D3 and B12, phenolic compounds, and highly digestible proteins with high biological value [3]. Wild fish follow diets rich in proteins (45-55%), fats (15-20%), fiber (8%), and mineral nutrients (10%). Fishmeal and fish oil are ideal for aquaculture due to their high protein content (60-72%), high digestibility (>95%), and essential amino acids, as well as valuable polyunsaturated fatty acids. However, their use accounts for 60-70% of operational costs in the industry [4] and requires about 16 of the 29 million tons of forage fish caught annually. Therefore, it is crucial to find sustainable alternatives that reduce the environmental and economic impact of aquaculture. The project aims to fortify animal feed to create functionalized fish filets, beneficial for the general population as well as those with specific chronic health conditions (e.g., cardiovascular and degenerative diseases, diabetes, cancer, gastrointestinal disorders) or temporary conditions (e.g., pregnant women). In this regard, the levels of fortifying ingredients in the final product will be determined according to the recommended intake levels set by LARN.The study focuses on the formulation of new fortified feeds, produced using by-products from agro-food chains, through the extraction and purification of compounds of interest using innovative, sustainable, and cost-effective techniques. Advanced analyses will evaluate the nutritional quality of the feeds and fish filets, both raw and cooked, using chromatography and mass spectrometry, with omics approaches to study proteins, metabolites, and lipids. Finally, the release and absorption of nutrients and functional compounds in the feeds and fish will be studied through bioaccessibility and bioavailability research. The importance of the project lies in ensuring a sustainable food supply, protecting public health, and optimizing the nutritional benefits of fish, while also addressing technological challenges related to feed fortification and fish fillet enhancement in farmed fish species.

REFERENCES

[1] The State of World Fisheries and Aquaculture 2020, FAO, 2020. https://doi.org/10.4060/ca9229en.
[2] EUMOFA., European Commission. Directorate General for Maritime Affairs and Fisheries., Study on the challenges of aquaculture products in food outlets., Publications Office, LU, 2024. https://data.europa.eu/doi/10.2771/967261 (accessed July 18, 2024).
[3] C.G. Awuchi, C.N. Chukwu, A.O. Iyiola, S. Noreen, S. Morya, A.O. Adeleye, H. Twinomuhwezi, K. Leicht, N.B. Mitaki, C.O.R. Okpala, BioMed Research International 2022 (2022) 1–18.
[4] S. Rimoldi, A.R. Di Rosa, R. Armone, B. Chiofalo, I. Hasan, M. Saroglia, V. Kalemi, G. Terova, Microorganisms 12 (2024) 744.

P009: FROM DOUBLE BONDS TO ACIDS: A GREEN WAY FOR CO VALORIZATION

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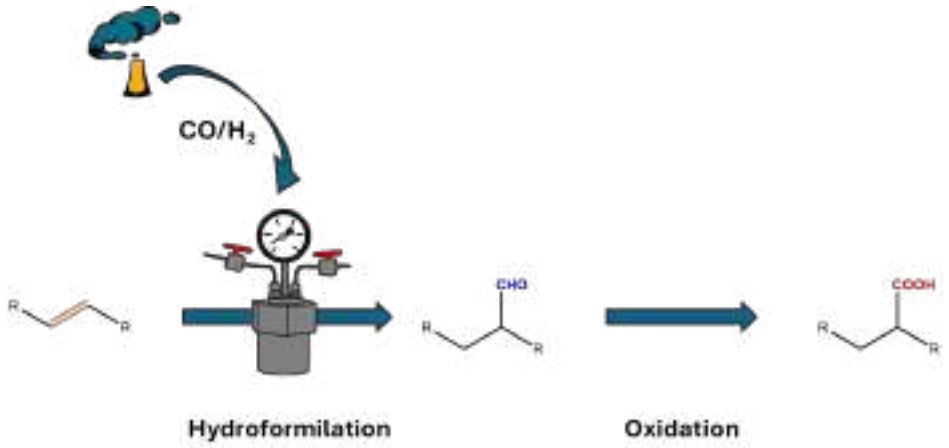
ABSTRACT

Hydroformylation, also known as the oxo process, is a metal-catalyzed reaction in which syngas (a mixture of carbon monoxide and hydrogen) reacts with olefins to produce aldehydes. Since its discovery at the beginning of the 20th century, hydroformylation has become one of the most important homogeneously catalyzed reactions in the chemical industry [1]. Most transition metals from groups 6 to 10 exhibit catalytic activity for this reaction, but cobalt and rhodium-based catalysts are the most effective. In particular, rhodium catalysts are the most widely used, offering reaction rates approximately 104 times faster than those of cobalt catalysts. In principle, hydroformylation can be made more sustainable by sourcing carbon monoxide from industrial emissions, thereby not only improving reaction efficiency but also reducing waste and minimizing the need for additional CO generation. This approach would contribute to a more environmentally friendly process. Despite its significance and versatility, hydroformylation presents challenges in terms of chemo-, regio-, and stereoselectivity. Side reactions such as hydrogenation and alkene isomerization can occur [2]. In the absence of symmetric substrates, the reaction typically produces a mixture of regioisomers, including both linear and branched products. The aim of this project, developed in collaboration with Polynt S.p.A., is to optimize the hydroformylation process for substrates derived from the company's value chain, focusing on improving efficiency and selectivity in the production of valuable aldehydes.



REFERENCES

[1] Zhang, B., Peña Fuentes, D. & Börner, A. Hydroformylation. *ChemTexts* **8**, 2 (2022).
[2] Vilches-Herrera, M., Domke, L. & Börner, A. Isomerization–Hydroformylation Tandem Reactions. *ACS Catal.* **4**, 1706–1724 (2014).

P010: ANALYTICAL CHALLENGES FOR DETECTION AND DETERMINATION OF SMALL MICROPLASTICS IN FOOD SAMPLES

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ABSTRACT

Microplastics (MPs) represent a growing concern as pollutants of anthropogenic origin, prompting the European Commission to advance legislation aimed at mitigating their potential risks to human health and the environment. To support effective decision-making and pollution control measures, there is a need for reliable, traceable and standardized methods for particle analysis that can provide consistent and comparable data. One of the main analytical challenges lies in detecting small microplastics (SMPs, 10-100 μm) in complex matrices, which often contain high levels of organic matter, without compromising particle integrity or altering polymer composition [1].
The present study focuses on the development and validation of a robust analytical approach for the chemical identification, physical characterization, and quantification of SMPs in drinking water and milk powder (infant formula) using Environmental Scanning Electron Microscopy (ESEM) [2] and μ-Raman spectroscopy. To maximize the impact of the research, both primary polystyrene and secondary polyethylene terephthalate particles were chosen as representative test materials. Preliminarily experiments on blank samples were carried out to establish best practices for clean room operations and procedures to minimize cross-contamination throughout the analytical process. A filtration system with 5 μm silicon filters was selected, achieving particle recovery between 85 and 120%, depending on particle size and the characterization technique. Additionally, different strategies for isolating SMPs from organic and inorganic matrix components were explored, including oxidative digestion and multi-enzymatic treatments combined with microwave-assisted alkaline hydrolysis [3]. Future work will include the analysis of real-world samples and participation in inter-laboratory proficiency testing as part of the ongoing funded project.

Acknowledgements: Plastic Trace Project JRP-EURAMET Call for Needs 2021-Green Deal. Project funded under the National Recovery and Resilience Plan (NRRP), Mission 4 Component 2 Investment 1.3 - Call for tender No. 341 of 15/03/2022 of Italian Ministry of University and Research funded by the European Union – NextGenerationEU Award Number: Project code PE0000003, Project title "Research and innovation network on food and nutrition Sustainability, Safety and Security – Working ON Foods" (ONFOODS)

REFERENCES

[1] Kadac-Czapska K et al., Food Chem., 440 (2024), 138246.
[2] Piergiovanni M et al., Molecules, 29 (2024), 3148.
[3] Da Costa Filho PA et al., Sci Rep., 11 (2021), 24026

P011: LIFE CYCLE ASSESSMENT (LCA) OF DIFFERENT PFAS REMOVAL TECHNIQUES FROM LANDFILL LEACHATE

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ABSTRACT

Per and poly-fluoroalkyl substances (PFAS) are a group of emerging organic contaminants that are receiving worldwide rising attention due to some peculiar chemical and physical characteristics that determine their well-spread use. Their high mechanic, chemical and heat resistance determined their success in the market as a pot surface covering, rain-proof clothing, additive in varnish and fire extinguishers and filler in PTFE articles but also causes their hazardousness: they are ubiquitous, persistent, bio-accumulative and toxic. Since landfilling remains one of the most frequent end-of-life scenarios of waste at the national level (20% of municipal solid waste and 51% of industrial waste)[1], landfills and leachates are one of the most important sources of PFASs in the environment, as well as represents a heavily polluted liquid fraction[2]. The aim of this study is to calculate the potential environmental impacts of different PFAS removal techniques from landfill leachate by performing a life cycle assessment (LCA) on laboratory preliminary tests. The analysed techniques are chemical-physical treatment (clariflocculation), clariflocculation with the presence of powdered active carbon (PAC) in a single (ss) and double-step (ds) process in different concentrations, and Fenton oxidation. The tests were performed on real leachate samples from Emilia-Romagna landfills. The results of the environmental footprint analysed (Global Warming Potential and Ecotoxicity) were normalized and presented according to different functional units (FU): 1m^3 of leachate and 1g of PFAS removed. The results obtained using SimaPro 9.5.0 as software, ReCiPe 2016 Midpoint (H) as the method and Ecoinvent 3 as the database, show that the most impacting phase of the treatments is the activated carbon (AC) production and its management. Important impact reductions were registered where the carbons recovery process was implemented (ds scenarios). Other important contributions are due to calcium hydroxide, polyelectrolytes and other chemicals production.

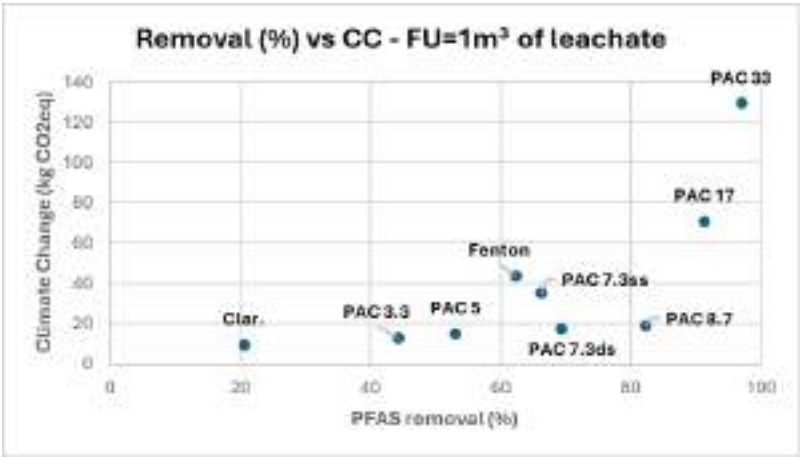

Figure 2: PFAS removal efficiency (%) vs Climate Change (CC) contribution for each technique according to 1m^3 of leachate as FU.

REFERENCES

[1] ISPRA: Catasto Nazionale Rifiuti, anno 2022, https://www.catasto-rifiuti.isprambiente.it/index.php?pg=gestnazione&advice=si
[2] Jia Li, Beidou Xi, Ganghui Zhu, Ying Yuan c, Weijiang Liu, Yi Gong, Wenbing Tan, A critical review of the occurrence, fate and treatment of per- and polyfluoroalkyl substances (PFASs) in landfills, Environmental Research 218 (2023) 114980.

P012: STUDY OF THE STRUCTURE OF ALTERED GLASSES IN AQUEOUS MEDIA COMBINING MOLECULAR DYNAMICS SIMULATIONS WITH HIGH-RESOLUTION SOLID STATE NMR SPECTROSCOPY

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ABSTRACT

Glasses are widely used to confine nuclear waste and their stability over geological timescales is therefore actively being investigated. This thesis focuses on the alteration in aqueous solution of three sodium aluminoborosilicates altered for different periods of time. The glasses are referred to as SBNA1, SBNA4 and SBNA6. Aluminium, sodium, and boron chemical environments have been studied both in the pristine glass and in the altered materials using high resolution solid-state NMR with MAS (sample Magic Angle Spinning), MQMAS (Multiple Quantum MAS) and REDOR (Rotation Echo DOuble Resonance) experiments. Computational simulations on the pristine glasses have been carried out using Molecular Dynamics (MD): structural models of the glasses were generated to study the speciations of different elements in these materials. Moreover, these structures were further optimized using Density Functional Theory (DFT) and the NMR parameters of all atoms were computed using Gauge Including Projected Augmented Wave (GIPAW).
The theoretical boron speciations in pristine glasses were compared with the experimental ones as obtained from ^{11}B NMR experiments, and a relationship was found between the fraction of four-folded boron BO_4 speciations, the isotropic chemical shift of sodium and the amount of non-bridging oxygens (NBOs) bonded to Na.
DFT and MD simulations of structural models of SBNA1, SBNA4 and SBNA6 showed that Al is mainly found in a four-folded form, the number of NBOs decreases from SBNA1 to SBNA6 (in agreement with experimental ^{23}Na NMR data) and the percentage of four-folded boron is close to the experimental one, except for SBNA4.
NMR data acquired on the altered glasses have been used to study the percentage of hydrated species (B, Al, Na) in the glass, by comparing the results obtained with REDOR and MAS experiments. According to the current knowledge for glass dissolution, sodium and boron are generally assumed to be completely removed from the altered layer that forms on the glass surface when in contact with water. Experimental NMR results in this thesis show residues of these elements can be found in the altered layer, at the interface with the pristine glass.

REFERENCES

[1] S. Narayanasamy, P. Jollivet, C. Jégou, M. Moskura, A. Abdelouas, T. Charpentier, and F. Angeli. Borosilicate glass alteration in vapor phase and aqueous medium. npj Materials Degradation, 6:86, 11 2022.
[2] T. Charpentier, M. C. Menziani, and A. Pedone. Computational simulations of solid-state NMR spectra: a new era in structure determination of oxide glasses. RSC Adv., 3:10550–10578, 2013.
[3] S. Gin, L. Neill, M. Fournier, P. Frugier, T. Ducasse, M. Tribet, A. Abdelouas, B. Parruzot, J. Neeway, and N. Wall, "The controversial role of inter-diffusion in glass alteration," Chemical Geology, vol. 440, pp. 115–123, 2016.

P013: EXPLOITING GLYCEROL: A SUSTAINABLE PATHWAY TO BENZIMIDAZOLE SYNTHESIS

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ABSTRACT

Benzimidazole compounds have recently gained notoriety in the illicit drug market as part of the growing class of New Psychoactive Substances (NPS). These synthetic compounds, particularly the nitazenes, exhibit potent opioid-like effects, despite their structural dissimilarity to traditional opioids. Preclinical studies suggest that nitazenes possess a high affinity for MOP opioid receptors, accounting for their potent analgesic activity.
The goal of this project was to explore green synthetic pathways to obtain a small library of Nitazenes. The primary focus was on utilizing glycerol as a green solvent, optimizing reaction conditions to minimize waste and enhance overall process efficiency [1].
The molecule scaffold shows a benzimidazole core featured by a N, N-diethyl-ethyl amine chain in position 1, a benzylic group with a para substituent in position 2 and a nitro group in position 5 (**Figure 1**).
The synthesis was based on obtaining these compounds through a sustainable way promoted by glycerol, reducing synthetic steps and minimizing purification steps as well, starting from 1-chloro-2,4-dinitro benzene, compared to the procedure reported in literature, which present several critical problems [2].
The synthetic pathway was focused on promoted the benzimidazole's cyclization between N-(2-diethylamino-ethyl)-4-nitrobenzene-1,2-diamine and a benzylic aldehyde by the glycerol, without any type of catalysts.
The developed synthetic protocol offers a practical, efficient, and environmentally friendly route to benzimidazole-based compounds. This methodology can be potentially extended to synthesize a broader range of structurally related compounds.

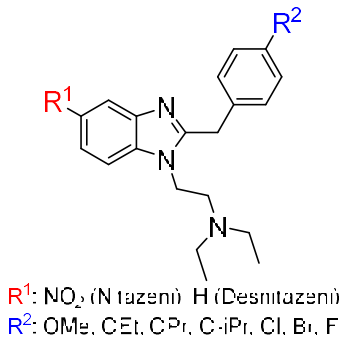

Figure 1. General structure of nitazene derivatives.

REFERENCES

[1] García, J. I.; García-Marín, H.; Pires, E. Glycerol Based Solvents: Synthesis, Properties and Applications. *Green Chem.* **2014**, *16* (3), 1007–1033
[2] Renton, P.; Green, B.; Maddaford, S.; Rakhit, S.; Andrews, J. S. NOpiates: Novel Dual Action Neuronal Nitric Oxide Synthase Inhibitors with μ-Opioid Agonist Activity. *ACS Med. Chem. Lett.* **2012**, *3* (3), 227–231.

P014: STRUCTURE AND ENERGETICS OF PET-HYDROLYZING ENZYME COMPLEXES: A SYSTEMATIC COMPARISON FROM MD SIMULATIONS

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ABSTRACT

Discovered in 2016, the enzyme PETase[1], secreted by bacterial *Ideonella Sakaiensis* 201-F6, has an excellent hydrolytic activity towards *poly*(ethylene terephthalate) (PET) at room temperature, while it decreases at higher temperatures due to the low thermostability[2]. Many variants have been engineered to overcome this limitation, that hinders industrial application. In this work, we investigate the binding characteristics of a tetrameric PET chain (PET4) to PETase wild-type (WT) and four mutants (DuraPETase[3], ThermoPETase[4], FastPETase[5], and HotPETase[6]) by means of standard molecular dynamics (MD) calculations, and free energy (FE) calculations. Our results indicate that PET4 forms stable complexes with the five enzymes at room temperature (~ 300 K); most of the interactions are localized close to the active site of the protein, where the W185 and Y87 residues interact with the aromatic rings of the substrate. Moreover, PET4 establishes aromatic interactions with the catalytic H237 residue, stabilizing the catalytic triad composed of residues S160-H237-D206, and helping the system to achieve an effective configuration for the hydrolysis reaction. Conversely, the binding affinity decreases at a higher temperature (~ 350 K), retaining moderate interactions only for HotPETase.

Furthermore, preliminary data on the energetics associated with the reaction mechanism of PETase WT are shown. A machine learning-based approach is used to achieve a valuable reaction coordinate to follow the transition[7]. To observe the breakage and formation of covalent bonds, the FE profiles of both the acylation and deacylation steps are calculated via QM/MM MD simulations at the DFTB3 level.

Our study offers valuable insights into the structural stability of these enzymes and the molecular determinants driving PET binding onto their surfaces, sheds light on the mechanistic steps that precede and govern the onset of hydrolysis and provides a foundation for future enzyme optimization[8].

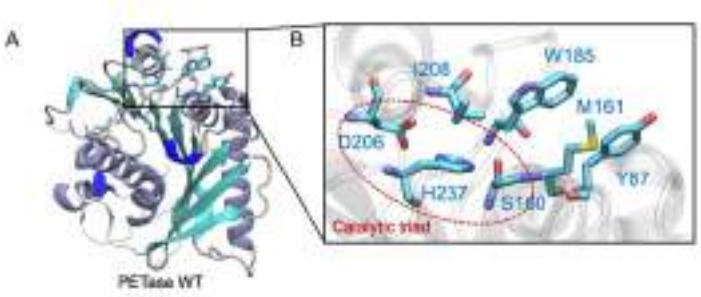

Figure. Structure of PETase WT. (A) Crystal structure of PETase WT (PDB ID: 5XJH). The secondary structure elements are colored in cyan for β-sheets, ice blue for α-helices, grey for β-turns, blue for 3_{10}-helices and white for loops. The two disulfide bonds and the residues forming the active site are shown in sticks. (B) Active site composed of the catalytic triad (S160, H237, D206), W185, Y87, M161 and I208 is highlighted in the close-up view reported on the right panel.

REFERENCES

[1] S. Yoshida, K. Hiraga, T. Takehana, I. Taniguchi, H. Yamaji, Y. Maeda, et al., *Science* **2016**, *351*, 1196.
[2] A. Amobonye, P. Bhagwat, S. Singh, S. Pillai, *Science of The Total Environment* **2021**, *759*, 143536.
[3] Y. Cui, Y. Chen, X. Liu, S. Dong, Y. Tian, Y. Qiao, et al., *ACS Catal.* **2021**, *11*, 1340.
[4] H. F. Son, I. J. Cho, S. Joo, H. Seo, H.-Y. Sagong, S. Y. Choi, et al., *ACS Catal.* **2019**, *9*, 3519.
[5] H. Lu, D. J. Diaz, N. J. Czarnecki, C. Zhu, W. Kim, R. Shroff, et al., *Nature* **2022**, *604*, 662.
[6] E. L. Bell, R. Smithson, S. Kilbride, J. Foster, F. J. Hardy, S. Ramachandran, et al., *Nat Catal* **2022**, *5*, 673.
[7] D. Mendels, G. Piccini, M. Parrinello, *J. Phys. Chem. Lett.* **2018**, *9*, 2776.
[8] A. Berselli, M. C. Menziani, F. Muniz-Miranda, *J. Chem. Inf. Model.* **2024**.

P015: REDESIGN OF SPYTAG/SPYCATCHER COMPLEX INTO ARTIFICIAL METALLOENZYMES. THE SPYTAG, OUR PLAYGROUND!

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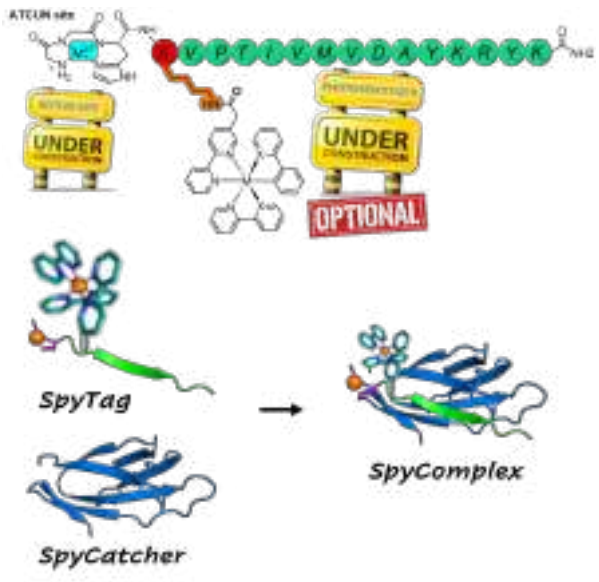
ABSTRACT

Metalloproteins promote several of the most complex biomolecular processes in Nature. The design of new metalloproteins is therefore of interest in the field of the development of new efficient biocatalysts. We present here results related to the redesign of the Spy protein into an artificial metalloenzyme. The Spy complex is an artificial protein system in which a peptide (SpyTag, ST) binds to a protein (SpyCatcher, SC) through an isopeptide bond, to give rise to a recombined Spy protein.[1] Design a metal site on the peptide component allow a straightforward introduction of metal binding sites on the final protein without redesigning the entire protein construct. Moreover, the peptides can be synthesized by solid-phase synthesis, making the SpyTag a playground where we can easily introduce different binding site for different metal ions, expanding the space of redesign of the Spy protein toward applications in industry, biotechnology and nanotechnology.

Today, we present a new copper protein designed using the SpyCatcher/SpyTag construct bearing a catalytic bis-histidine site, capable to bind copper in both +1 and +2 oxidation states and to promote reactions of oxidation of catechols. These results have prompted us to try to achieve stereoselectivity in L/D-DOPA oxidation, which will be discussed. Moreover, today we are happy to show how the same sequence of SpyTag can be functionalize with a different active site and a photosentitizer on a side chain allowing us to achieve a new artificial metalloenzyme for photocatalytic reactions.

Briefly, this plethora of SpyTag/SpyCatcher adducts will make the SpyTag peptide our playground where to create tailored SpyComplex for specific reactions!



Project "Artificial enzymes for the photocatalytic production of hydrogen in photosynthetic bacteria" National Recovery and Resilience Plan (NRRP), M2 C2 Inv. 3.5 funded by the European Union – NextGenerationEU. Project RSH2A_000009, C.D. 445 29/12/2022 Italian Ministry of Environment and Energy Security. "Bando di Ateneo per la Ricerca 2022" – A Way Towards Artificial Metalloenzymes - University of Parma.

REFERENCES

[1] S. C. Reddington, M. Howarth, Curr. Opin. Chem. Biol. (2015), 29, 94–99.

P016: FOOD COLD-CHAIN MONITORING WITH AN INNOVATIVE EGT-BASED TIME-TEMPERATURE INTEGRATOR

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ABSTRACT

Monitoring temperature along the food cold-chain is critical to guarantee food quality and safety for consumers.
Any break in the cold chain, such as temperature deviations, can compromise the safety and freshness of the products, leading to food spoilage and even health risks. Smart packaging[1] and temperature-monitoring devices such as time-temperature integrators[2] (TTIs) are becoming important in the cold chain to enhance control, reduce waste, and ensure the efficiency of the system. In the view of the FRUALGAE European Project, we developed an innovative TTI based on an Electrolyte Gated based on the organic semiconductor Poly[2,5-(2-octyldodecyl)-3,6-diketopyrrolopyrrole-alt-5,5-(2,5-di(thien-2-yl) thieno [3,2-b] thiophene)] (simply known as DPP-DTT) on interdigitated gold electrodes. The semiconductor is in contact through an agar based electrolyte with a gate electrode made of a conductive hydrogel, composed of reduced graphene oxide and PEDOT:PSS[3]. The time-temperature irreversible response of the device is based on the different water evaporation kinetics of the hydrogel when exposed to various environmental conditions in terms of temperature and atmosphere, which in turn influences how the gate can modulate the device based on the exposure time and exposure conditions. The transconductance signal enables us to discern the time of exposure and exposure conditions of the hydrogel. After further optimization and integration in food packaging, the device could be in principle used to determine the temperature history of fresh food.

REFERENCES

[1] S. Chen, S. Brahma, J. Mackay, C. Cao, e B. Aliakbarian, «The role of smart packaging system in food supply chain», *Journal of Food Science*, vol. 85, fasc. 3, pp. 517–525, 2020, doi: 10.1111/1750-3841.15046.
[2] K. P. Koutsoumanis e M. Gougouli, «Use of Time Temperature Integrators in food safety management», *Trends in Food Science & Technology*, vol. 43, fasc. 2, pp. 236–244, giu. 2015, doi: 10.1016/j.tifs.2015.02.008.
[3] F. Zhang *et al.*, «Multi-modal strain and temperature sensor by hybridizing reduced graphene oxide and PEDOT:PSS», *Composites Science and Technology*, vol. 187, p. 107959, feb. 2020, doi: 10.1016/j.compscitech.2019.107959.

P017: NEW INSIGHTS INTO THE KEY ROLE OF THE THERMAL TREATMENT OF V/P/O CATALYSTS FOR THE SELECTIVE OXIDATION OF BUTANE TO MALEIC ANHYDRIDE

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ABSTRACT

Maleic anhydride (MA) is a versatile molecule due to its three active sites, i.e. two carboxylic groups and a double carbon bond. It is considered an important building block in industrial chemistry, with several applications such as monomers for polyesters and alkyd resins, as well as an intermediate to produce fine chemicals (succinic acid, malic acid, and fumaric acid). Industrially, the production of MA remains solidly linked to the continuous-flow, gas-phase selective oxidation of petrochemical raw materials, Traditionally, benzene was the main substrate used in the production of MA, using vanadium and molybdenum containing catalysts. However, this method presents several drawbacks such as the carcinogenic nature of benzene itself, relatively low atom efficiency (i.e. two C atoms are lost in the form of COx), and high exothermicity. [1] Therefore, benzene is gradually being replaced with *n*-butane (due to lower cost and higher atom economy), while vanadium and molybdenum catalysts have been replaced by vanadium phosphates (V/P/O), which are able to promote the selective oxidation of this linear alkane toward MA exhibiting best results in terms of conversion and yields. [2]
This work explores the thermal treatment of V/P/O catalyst precursors to achieve active and selective catalysts for the oxidation of *n*-butane to maleic anhydride (MA) in a continuous-flow, fixed-bed reactor. Vanadyl pyrophosphate (V^{4+}, VPP), the key catalyst component, is produced together with suitable V^{5+} vanadium orthophosphate ($VOPO_4$) allotropic forms by thermally treating vanadyl hydrogen phosphate hemihydrate (VHP) in various atmospheres and temperature ramps. The characterization conducted using X-ray diffraction, Raman spectroscopy, and reaction testing allowed the identification of optimal conditions for active and selective catalysts. Oxygen is necessary for obtaining VPP and affects the vanadium oxidation state, a crucial parameter for selectivity. Water enhances the crystallinity and conversion of VHP to VPP. An optimized calcination atmosphere (6:10:84 mol% of O_2:H_2O:N_2) ensures 70% MA selectivity at 50% butane conversion at 400 °C. VHP precursors characterized by higher P/V ratios allow to obtain higher MA selectivity when treated at the same calcination conditions.
This study aims to ensure the consistent production of the best-performing catalyst by tuning the calcination conditions based on the precursor's specific pre-calcination characteristics and properties.

REFERENCES

[1] Cavani, F.; Trifirò. F. Some Innovative Aspects in the Production of Monomers via Catalyzed Oxidation Processes. Appl. Catal. A 1992, 88 (2), 115–135.
[2] Abon, M.; Volta, J.-C. Vanadium Phosphorus Oxides for N-Butane Oxidation to Maleic Anhydride. Appl. Catal. A Gen 1997, 157 (1–2), 173–193.

P018: ELECTROCHEMICAL NICKEL-CATALYZED BENZYLATION OF TROPONES

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ABSTRACT

Synthetic organic electrochemistry (*eChem*) is nowadays one of the most promising tools to realize redox processes by replacing stoichiometric oxidizing/reducing chemical agents with "*green electrons*".[1] At the same time, *Nickel catalysis* has become a benchmark tool for the realization of *cross-electrophile couplings* due to a facile access to multiple oxidation states and a fast oxidative addition.[2]

We have developed a novel electrochemical cross electrophile coupling of Aryl-Tropones **1** with benzaldehyde derivatives **2**[3] using Nickel Complex as a convenient organometallic catalyst.[4] Under *galvanostatic* conditions and employing the *sacrificial anode technique*, a wide range of α-α' disubstituted Tropones **3** derivatives were formed. The selectivity of the protocol is dictated by the peculiar reactivity of the free α' position in α-substituted Tropones, wich is the most electrophilic due to the resonance effects exerted by ketone functionality (***Figure 1***).

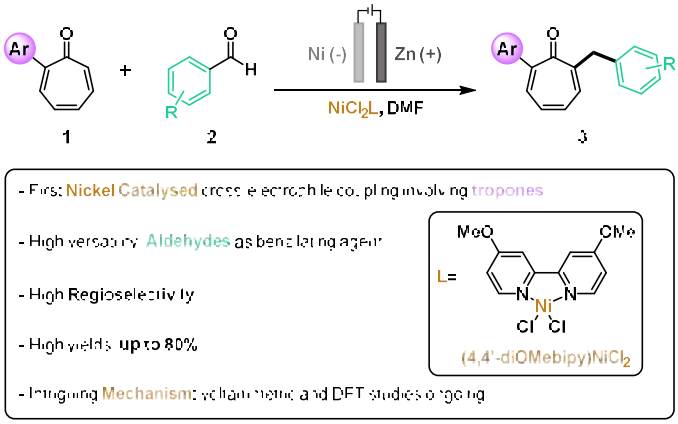

Figure 1. Electrochemical Nickel-Catalyzed Benzylation of Tropones

REFERENCES

[1] Wiebe, A.; Gieshoff, T.; Möhle, S.; Rodrigo, E.; Zirbes, M.; Waldvogel, S.R. *Angew. Chem. Int. Ed.*, **2018**, *57*, 5594.

[2] Tasker, S.Z; Standley, E.A.; Jamison, T.F. *Nature*, **2014**, *509*, 299-309.

[3] Brunetti, A.; Garbini, M.; Zanardi, C.; Bertuzzi, G., Bandini, M., *Results Unpublished*.

[4] Montgomery, J., *Angew.Chem.Int.Ed.* **2004**, *43*, 3890 – 3908

P019: MECHANOCHEMISTRY: A SELECTIVE TOOL FOR THE SYNTHESIS OF METAL COMPLEXES

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ABSTRACT

Mechanochemistry, defined by IUPAC as "any chemical reaction induced by the direct absorption of mechanical energy," has earned a place among the "Ten Chemical Innovations That Will Change Our World" [1]. Its appeal lies in its low environmental impact, enabled by significant solvent reduction, and in its capacity to access compounds otherwise unattainable through conventional methods [2]. The mechanochemical synthesis of molecular metal complexes is well-documented and increasingly popular due to these benefits, including reduced solvent use, accelerated reaction kinetics, and improved sustainability. Yet, mechanochemical reactions are often perceived as unpredictable and highly heterogeneous, giving rise to the notion that products form more by chance than through a well-defined pathway. To challenge this perception, we set out to demonstrate that mechanochemistry can achieve clean, rapid, and selective reactions, particularly in synthesizing metal complexes with monodentate ligands, where chelation is absent.
In this study, we synthesized a series of heteroleptic mononuclear complexes using pyridine and a substituted benzoic acid as ligands, achieving distinct coordination geometries under varying mechanochemical conditions. When hydrated zinc acetate was used, the reaction led to the formation of an octahedral water-coordinated complex, while using anhydrous zinc acetate plus "dry milling" conditions yielded a tetrahedral complex. This outcome highlights not only the adaptability of mechanochemistry in controlling product geometry but also its unique capacity to produce moisture-sensitive products without requiring specialized setups, such as Schlenk lines, gloveboxes, or dry solvents. By enabling such control in a simplified, solvent-free environment, mechanochemistry offers a practical and environmentally friendly alternative to traditional synthetic routes for air- or moisture-sensitive compounds.
Building on these findings, we then replaced pyridine with isonicotinamide as the ligand. This substitution led, unexpectedly, to the selective formation of hexanuclear assemblies, underscoring mechanochemistry's potential to drive complex self-assembly in a controlled, selective manner. The ability to access such higher-order structures from simple starting materials and without solution-based protocols expands the scope of mechanochemical synthesis, offering new avenues for the sustainable, scalable production of complex metal-organic architectures.

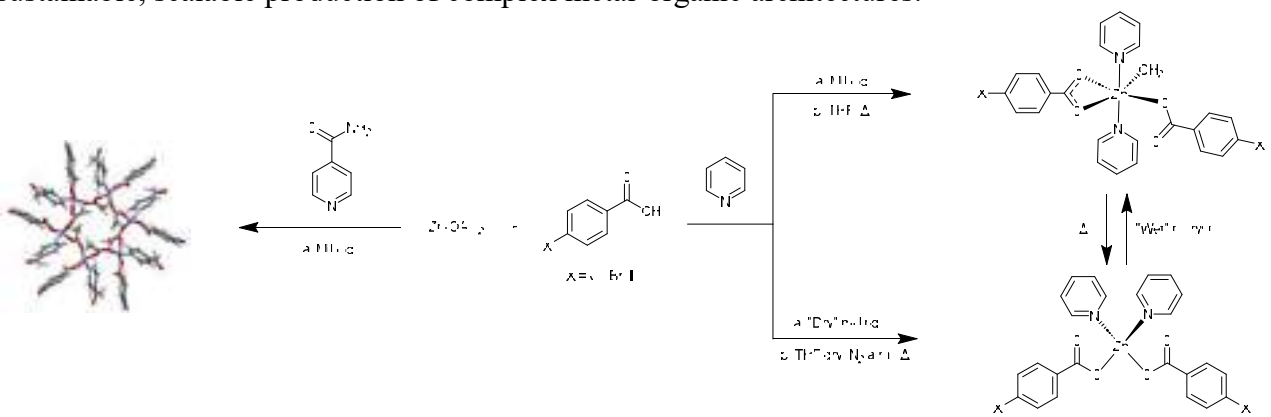

Figure 1. Synthetic pathway displaying the complexes obtained throughout our study

REFERENCES

[1] Fernando Gomollón-Bell, Chemistry International 2019, 41, 12– 17.

[2] Tomislav Friščić, Cristina Mottillo, and Hatem M. Titi, Angewandte Chemie Int. Ed. 2020, 59, 1018–1029.

P020: WATER SPLITTING GOES CHIRAL: MHOF FOR SPIN SELECTIVE H_2 PRODUCTION

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ABSTRACT

Today our society depends on energy production to perform any kind of activity. The problems that arise from the use of fossil fuels are well known and renewable sources, widely increased in recent years, are not without their flaws. One of the most interesting approaches to solve these problems is to turn the excess of sustainable electricity into chemical energy through electrochemical splitting of water (EWS). This is an environmentally friendly process for hydrogen production, which can be stored and/or used independently instead of fossil fuels [1].
In commercial electrolyzers, the EWS reaction occurs at a potential considerably higher than the theoretical value of +1.23 V [1]. Oxygen evolution reaction (OER) is the limiting factor in the EWS process since it requires 4-electron transfer and requires high overpotentials to counteract its inherently slow kinetics. At present, the most efficient catalysts for this reaction are based on Platinum, Iridium and Ruthenium which are precious and rare metals.
One possible strategy to improve OER reaction using more common and less expensive materials is through the Chirality Induced Spin Selectivity (CISS) effect [2]. As can be seen in Figure 1, due to the CISS effect chiral organic molecules can act as spin filters and produce oxygen in its fundamental state (triplet) with maximum efficiency and with a full selectivity.
We decided to use chiral Metal-Hydroxide Organic Frameworks (MHOFs) as spin-selective catalysts for OER. This kind of frameworks have been widely studied in the last years as catalysts for EWS because of their large surface area, high porosity and well-defined structure [3].
We will present results related to the study of catalytic performances of different Nickel-based MHOFs characterized by different types of organic linkers.

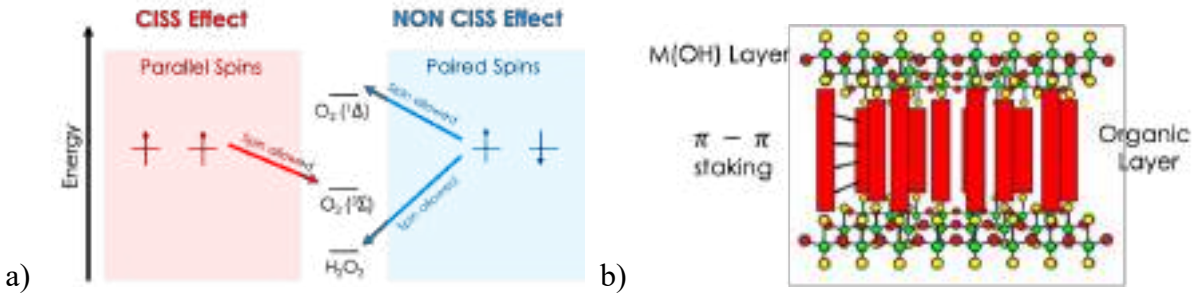

Figure 1 a) Principle of CISS and non-CISS processes in OER and b) Structure of a MHOF

REFERENCES

[1] Raveendran A, Chandran M, Dhanusuraman R. *A comprehensive review on the electrochemical parameters and recent material development of electrochemical water splitting electrocatalysts*. RSC Adv, 2023,13(6):3843-76
[2] Waldeck DH, Naaman R, Paltiel Y. *The spin selectivity effect in chiral materials*. APL Mater, 2021, 9(4):040902
[3] Yuan S, Peng J, Chai B, *Tunable metal hydroxide–organic frameworks for catalysing oxygen evolution*, Nature Materials, 2022, 21(6): 673-680

P021: DEVELOPMENT OF LUMINESCENT BIOPOLYMER PROBES FOR MICRO- AND NANOPLASTICS

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ABSTRACT

Plastic pollution is rising dramatically due to human activities; in particular, the plastic fragments below 5 mm – the so-called micro- and nanoplastics (MNPs) – are ubiquitous: in water, sediments, soil, and air. Their small dimensions make them more easily bioavailable and ingestible by animals, reaching humans through the food chain. The detection of MNPs is a great challenge since existing protocols are unsatisfactory for microplastics and mostly absent for nanoplastics. In this framework, fluorescence-based methods could represent a possible solution for MNPs identification and quantification, since they are fast, easy, cheap, and sensitive. Fluorescence has found application in identifying plastic debris using fluorescence microscopy after staining them with suitable dyes, such as Nile Red (NR), which has proven to be a valuable choice for staining different types of microplastics in water [1]. However, its inclination to aggregate in aqueous environment can lead to the emergence of fluorescent objects that can be mistaken for MNPs, causing "false positives" [2].
To avoid this problem, which often affects molecular lipophilic dyes used for MNPs staining, one strategy could be the conjugation of a fluorophore to a biopolymer soluble in water, such as hyaluronic acid (HA). Functionalizing HA with a fluorophore, even in very small amounts, alters its colloidal behavior, solubility and photophysical features [2]. The resulting properties can be controlled by acting on the fluorophore nature and amount.
With this purpose, we synthesized and characterized in its photophysical properties a hyaluronic acid with a derivative of Nile Red. This results in a fluorogenic material, with a very weak emission intensity in water, but that can recover its brightness when adsorbed onto MNPs (Fig. 1). Preliminary studies show that HA-NR exhibits high affinity for various types of MNPs, making them luminescent and detectable by confocal microscopy. Moreover, fluorescence lifetime imaging (FLIM) can enable a discrimination of MNP nature based on the average lifetime of the adsorbed probe.

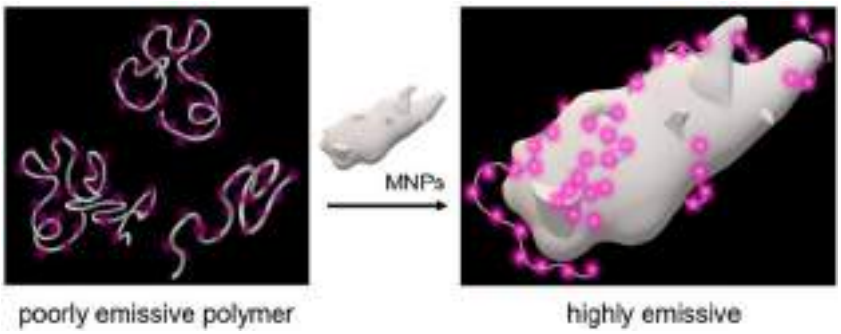

Figure 1. Schematized interaction between HA functionalized with Nile Red and MNPs.

REFERENCES

[1] Chiara Capolungo, Damiano Genovese, Marco Montalti, Enrico Rampazzo, Nelsi Zaccheroni, Luca Prodi, *Chem. Eur. J.*, **2021**, *27*, 17529–17541.
[2] Matteo Cingolani, Damiano Genovese, Enrico Rampazzo, Nelsi Zaccheroni, Luca Prodi, *Environ. Sci.: Nano*, **2022**, *9*, 582–588.

P022: Δ^9-TETRAHYDROCANNABIPHOROL: IDENTIFICATION AND QUANTIFICATION IN RECREATIONAL PRODUCTS

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ABSTRACT

Δ^9-Tetrahydrocannabinol (Δ^9-THC) is the component of the cannabis plant responsible for the psychoactive effects through the activation of the endocannabinoid receptor 1 (CBR1). Following extensive structure–activity relationship (SAR) studies on it, new molecules with increased CBR1 affinity were synthesized over the last decades. Recently, the knowledge arising from these pharmacological and synthetic investigations has been extensively used by the industry of substances for recreational use also thanks to the 2018 Farm Bill Act in the USA and the incentive for low-THC cannabis (hemp) cultivation in Europe, which have boosted the availability of hemp derived precursors. As a result, new semi-synthetic natural and pseudo natural cannabinoids related to the most famous Δ^9-THC and often not subjected to legal restrictions are now available in the online market in a broad array of retail products with no preventive study on their pharmacodynamics and pharmacokinetics [1]. Some of these products (gummies, cannabis flower and a vape cartridge), declared to contain the most potent among all the known cannabinoids, Δ^9-Tetrahydrocannabiphorol (Δ^9-THCP) [2], were tested through ultra-high-performance liquid chromatography system coupled with high-resolution orbitrap mass spectrometry (UHPLC-HRMS) to determine the effective amount of Δ^9-THCP and of other cannabinoids. All the three samples were found to contain Δ^9-THCP in amounts significantly different from those declared by the producer. Moreover, the application of an untargeted metabolomics approach (cannabinomics) enabled the identification of other cannabinoids including the emerging semi-synthetic hexahydrocannabinol (HHC) and tetrahydrocannabidiol (H4-CBD) together with byproducts of synthetic origin.

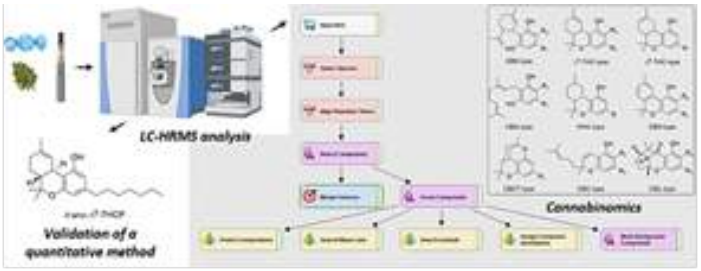

Figure 1. Graphical abstract

REFERENCES

[1] Caprari et al. An emerging trend in Novel Psychoactive Substances (NPSs): designer THC Journal of Cannabis Research (2024) 6:21, https://doi.org/10.1186/s42238-024-00226-y. [2] Citti et al., A novel phytocannabinoid isolated from Cannabis sativa L. with an in vivo cannabimimetic activity higher than Δ9-tetrahydrocannabinol: Δ9-Tetrahydrocannabiphorol, Sci. Rep. 9 (1) (2019) 20335, https://doi.org/10.1038/s41598-019-56785-1.

This work was funded by Fondo Di Ateneo Per La Ricerca Anno 2024 (FAR2024PD), A.D06@FAR2024_DIP@05FA-CANNAZZA_FARDIP_2024.

P023: KINETIC AND SUBSTRATE SPECIFICITY DETERMINATION OF BACTERIAL LPMO

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ABSTRACT

Lytic polysaccharide monooxygenases (LPMOs) are copper enzymes discovered in the last decade. Their importance in the degradation of recalcitrant substrates in sustainable processes is now well established, however the catalytic peroxygenase mechanism has yet to be fully understood. This is also because the study of reaction kinetics has to deal with multiple variables, including the nature of the substrates, the presence of unwanted side reactions and the low protein stability in the presence of H2O2 as a co-substrate. In this work, three bacterial LPMOs from the AA10 family were investigated: Pseudomonas putida AA10 (PpAA10), Streptomyces coelicolor AA10B (ScAA10B) and AA10C (ScAA10C). Their activity against specific substrates was initially evaluated by an ATR-FTIR assay[1] for a qualitative characterization, and then to determine electrochemically their kinetic constants an amperometric assay[2] based on the detection of the H2O2 consumption was used (Figure). This allowed the determination of turnover numbers (TN) and total turnover numbers (TTN) on different substrates. The best performance was obtained with ScAA10C and ScAAA10B on nanocrystalline cellulose with a TN of 3.81 s-1 and 2.88 s-1, respectively, and a TTN of 1208 and 735, respectively, PpAA10 is active on β-chitin with a TN of 1.02 s-1 and a TTN of 61, providing a valuable insight into their substrate specificity and stability[3]. The enzyme stability over time increases on more crystalline substrates and in the presence of the carbohydrate-binding module (CBM), yielding activity values comparable to those for fungal LPMOs. Moreover, the presence of CBM resulted in more efficient consumption of H2O2 by LPMO, leading to improved enzymatic activity and increased resistance to oxidative inactivation.

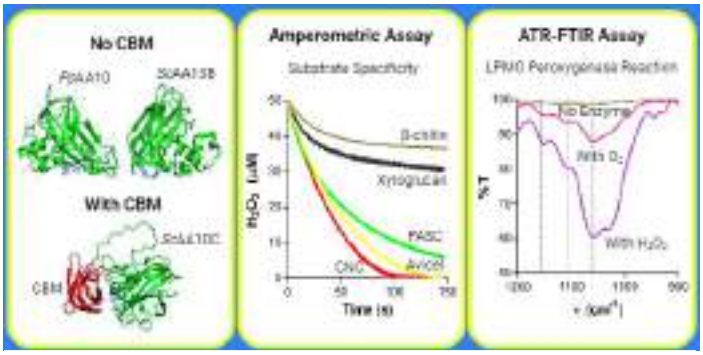

Figure 1. Table of contents of the proposed work.

REFERENCES

[1] Serra, I.; Piccinini, D.; Paradisi, A.; Ciano, L.; Bellei, M.; Bortolotti, C. A.; Battistuzzi, G.; Sola, M.; Walton, P. H.; Di Rocco, G. Activity and Substrate Specificity of Lytic Polysaccharide Monooxygenases: An <scp>ATR FTIR</Scp> -based Sensitive Assay Tested on a Novel Species from Pseudomonas Putida. Protein Science 2022, 31 (3), 591–601. https://doi.org/10.1002/pro.4255.

[2] Schwaiger, L.; Csarman, F.; Chang, H.; Golten, O.; Eijsink, V. G. H.; Ludwig, R. Electrochemical Monitoring of Heterogeneous Peroxygenase Reactions Unravels LPMO Kinetics. ACS Catal 2024, 14 (2), 1205–1219. https://doi.org/10.1021/acscatal.3c05194.

[3] Carletti, A.; Csarman, F.; Sola, M.; Battistuzzi, G.; Ludwig, R.; Di Rocco, G. Kinetic and Substrate Specificity Determination of Bacterial LPMOs. ACS Catal 2024, 14586–14594. https://doi.org/10.1021/acscatal.4c04510.

P024: BIOACTIVE COMPOUNDS FROM NON-PSYCHOACTIVE *CANNABIS SATIVA* L. AS INNOVATIVE THERAPEUTIC AGENTS AGAINST CANCER CELL PROLIFERATION

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ABSTRACT

Cannabis sativa L. is a plant with a very complex chemical composition It includes both psychoactive and non-psychoactive (hemp) varieties, based on the cannabinoid profile. Particularly, hemp is characterized by a low level of Δ^9-tetrahydrocannabinol (Δ^9-THC), typically below 0.3%, and high levels of cannabidiol (CBD). CBD has already demonstrated to possess diverse biological activities. Moreover, several studies have highlighted its antiproliferative activity on different cancer cell lines, even if its mechanism/s of action is still under investigation [1,2]. In addition to cannabinoids, hemp contains other chemical classes of bioactive compounds, such as polyphenols [3]. Cannflavins are the typical isoprenoid flavones of *C. sativa*, with cannflavin A and B (CFL-A and CFL-B) as most representative bioactive ones [3,4]. However, there are still few studies of their antiproliferative properties, making the investigation on their bioactivity a relevant topic.

In the light of all the above, the aim of this project was to obtain and fully characterize a cannabinoid- and a polyphenols-enriched fraction (namely CEF and PEF, respectively) from hemp inflorescences, using targeted and untargeted UHPLC-HRMS analysis, and to assess their activity against cancer cells with *in vitro* cell-based assays.

As for cannabinoids, CEF and CBD were tested for their ability to decrease the cell viability, migration and proliferation of glioblastoma multiforme (GBM) U87MG and T98G cancer cell lines. To achieve this, diverse bioassays were performed. Initially, CEF and CBD demonstrated to be able to decrease cell viability with IC_{50} values lower than the chemotherapy drug temozolomide. Secondly, two different cell migration assays were performed, *i.e.* cell tracking and wound healing assay. CEF and CBD were able to significantly reduce cell motility and proliferation in both cell lines compared to control cells. Then, plate colony assay was performed, and both continuous treatment and pre-treatment alone with CBD caused a significant decrease in the formation of new cell colonies, compared to control. The existence of a possible new target for CBD, involved in cell mobility and migration is plausible. Now the research is focused to a deeper investigation of the mechanism/s of action of cannabinoids, with a focus on CBD.

As for more polar compounds, *i.e.* polyphenols, PEF was obtained with a newly optimized extraction and purification method. The extract and pure compounds were then tested for their ability to decrease the cell viability of colorectal cancer (CRC) Caco-2 and SW480 cell lines, with promising results, in comparison with the chemotherapy drug cisplatin, even if further research is needed to elucidate their mechanism of action.

REFERENCES

[1] F. Pellati, *et al.* BioMed Res. Int. 2018 (2018) 1–15. https://doi.org/10.1155/2018/1691428

[2] L. Anceschi, *et al*. Phytother. Res. 36 (2022) 914–927. https://doi.org/10.1002/ptr.7357

[3] F. Pollastro, *et al.* Curr. Med. Chem. 25 (2018) 1160–1185. https://doi.org/10.2174/0929867324666170810164636

[4] J.L. Bautista, *et al.* ACS Omega 6 (2021) 5119–5123. https://doi.org/10.1021/acsomega.1c00318.

P025: LIPOSOME NANOFIBROUS HYDROGEL FOR THERANOSTIC APPLICATIONS

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ABSTRACT

Metastases are developed in 45-50% of soft tissue sarcoma (STS) and melanoma patients, leading to reduced quality of life and high mortality. Standard first-line therapies often fail to control metastasis and cause systemic toxicity [1]. In this project we aim at developing a system that is able to give mechanical support to the soft tissue of a patient after a surgical procedure and also to prevent the relapse of the tumor mass thanks to the in-situ release of antitumoral drug. We use an electrospun fibre mat (polymeric matrix) in order to give to the system structural rigidity and to have a high surface area to absorb the hydrogel-like medium where the antitumoral drug vector are embedded. To deliver the antitumoral drug we exploit Large Unilamellar Vesicles (LUV) which are highly exploited in literature for their low toxicity, good biocompatibility good pharmacokinetics and ease of synthesis [2]. In order to be able to follow the LUV fate inside this polymeric matrix we fluorescently stained the LUV and we studied the system via confocal microscopy coupled with Fluorescence Lifetime Imaging Microscopy (FLIM). These two high-resolution techniques, providing extensive molecular insights, allowed us to study the interaction of the free molecular fluorescent probe with the above-mentioned polymeric matrix and to compare it with the interaction of the fluorescent-tagged LUV with the polymeric matrix. These studies successfully showed that the fluorescent-tagged LUV retain their properties inside the polymeric matrix.

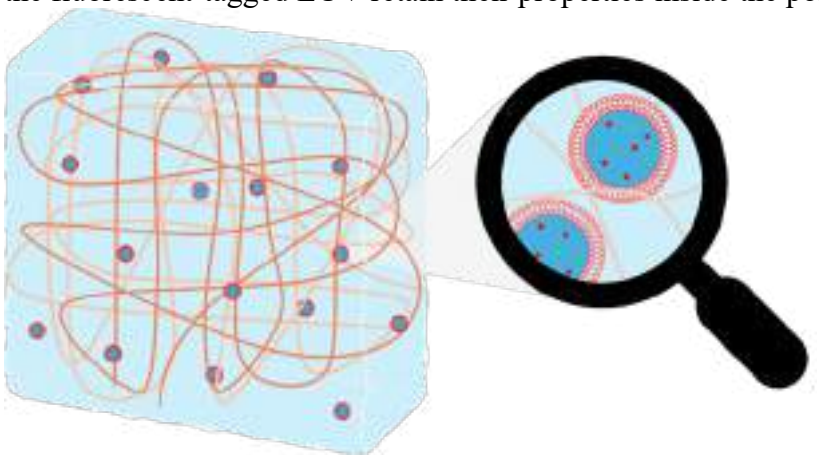

Figure 1. schematic representation of the system: LUV embedded in a polymeric matrix composed of an electrospun fibre mat and a hydrogel-like medium

REFERENCES

[1] A. Italiano, " Trends in survival for patients with metastatic soft-tissue sarcoma," Cancer, Volume117, Issue5, 1049-1054, 2010.
[2] X. Zhao, "Application of Non-Viral Vectors in Drug Delivery and Gene Therapy", Polymers (Basel), 13(19) 3307-3335, 2021.

P026: HYDROGEN AND CARBON USE THROUGH ENERGY FROM RENEWABLES

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ABSTRACT

Hydrogen and CCUS are recognized by the European Commission and in Horizon Europe as transversal themes with high potential to achieve the objectives of the Green Deal and neutrality in climate-changing emissions by 2050. In particular, both technologies are attributed a significant role in the decarbonization of "Hard to Abate" industrial sectors such as chemicals, steel, materials and fertilizers production Furthermore, hydrogen is believed to play a strategic role in obtaining energy carriers to be used in heavy transport and long distance starting from railway and naval ones, both directly (LH) and through derived e-fuels (NH_3, CH_4, liquid fuels). In many of these areas, the use of hydrogen is associated with the capture and use/storage of CO_2 and the production and transformation of renewable energy. The University of Bologna and Eni are developing in Ravenna a Joint Research Laboratory dedicated to Hydrogen and Carbon use through Energy from Renewables. This research lab is centered on three interconnected pillars, in strong partnership with the new investments in the decarbonization sector present in the area:

- Sustainable and safe production and use of hydrogen
- Capture, Use Storage of CO_2 in synergy with the transformation of hydrogen
- Technologies with potentially negative CO_2 emissions

The initiative addresses the creation of a strategic innovation laboratory on the production and use of hydrogen and on the capture and use of CO_2 that accompanies the projects of international importance present on the territory. A place to encourage close collaboration between public and private sectors for the development of technologies capable of shortening the time to market of innovative solutions.

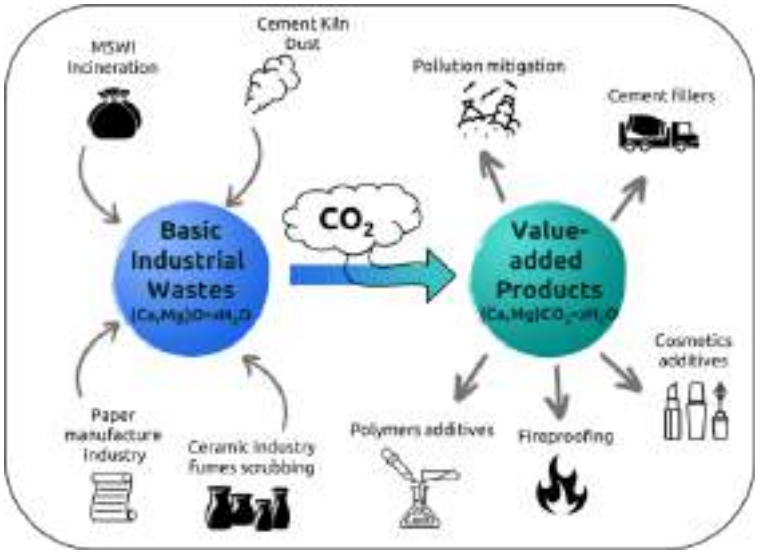

Figure 1 - CO_2 capture and utilization – Mineralization over industrial wastes.

P027: DUAL-LOADED Ce-DOPED BIOACTIVE GLASSES: AN INNOVATIVE APPROACH FOR ENHANCED ANTIOXIDANT AND REGENERATIVE PROPERTIES

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ABSTRACT

Bioceramics, especially bioactive glasses (BGs), are widely used in biomedical applications for *hard tissue* regeneration and *wound healing*.[1,2] Current research seeks to enhance BGs performance by improving biological properties and inducing targeted effects at implant sites, either by doping with therapeutic inorganic ions (TIIs), like cerium, or loading with biomolecules and drugs.[2] Cerium-doped BGs (Ce-BGs) show antioxidant properties similar to catalase (CAT) and superoxide dismutase (SOD) enzymes, helping to reduce inflammation by limiting ROS production.[3] Mesoporous bioactive glasses (MBGs) are particularly effective as drug delivery systems (DDSs) due to their high pore volume and specific surface area, allowing efficient loading of organic molecules.[3] This study explores Ce-MBGs loaded with various polyphenols: Quercetin (Q), Morin hydrate (M), 3-Hydroxyflavone (F), and a mixture of polyphenols extracted from chestnuts flour (POLY); additionally, the loading with two different drugs, Ibuprofen (IBU) and Paracetamol (PARA), was evaluated. To create a *dual-loaded* system able to combine the properties of different biomolecules, Ce-MBGs loaded with polyphenols and drugs were mixed in a 1:1 ratio. We then evaluated the antioxidant properties and the ability of these *dual-loaded* systems to form a hydroxyapatite (HA) layer after soaking in simulated biological fluid (SBF). The studied glasses included MBG (without cerium) and MBG3.6 (containing 3.6 mol% CeO_2).

Our findings show that polyphenols significantly enhance SOD-[illegible] Ce-MBGs exhibiting around 90% antioxidant efficiency, unaffected by the presence of the drugs. Polyphenols also impart CAT-mimetic properties to undoped MBGs, while MBG3.6 exhibits CAT-like activity of 100% already, thanks to the presence of Ce, and the loading with drugs does not inhibit this performance. After 14 days in SBF, *dual-loaded* Ce-MBGs formed an HA layer, indicating sustained bioactivity even after loading. SEM-EDS (Figure 1, red circles) and XRPD analyses confirmed HA formation, with characteristic peaks aligning with JCPDS 00-009-0432.[4]

Figure 1. SEM micrograph of MBG3.6-Q-IBU after 14 days of soaking in SBF.

In conclusion, a 1:1 mixture of Ce-MBGs loaded with polyphenols and either Ibuprofen or Paracetamol presents a promising system combining the unique benefits of each biomolecule with the properties of the unloaded MBGs. All *dual-loaded* samples exhibited high SOD and CAT-like activities and the capacity to form an HA layer, indicating their potential for dual-use as DDSs and regenerative agents in *hard tissue* applications.

REFERENCES

[1] Hench L L; The story of Bioglass®; J. Mater. Sci. Mater. Med. 17 (2006) 967–978.

[2] Mehrabi T, Mesgar A S, Mohammadi Z; ACS Biomaterials Science & Engineering 2020 6 (10), 5399-5430

[3] Lusvardi G, Fraulini F, D'Addato S, Zambon A; Loading with Biomolecules Modulates the Antioxidant Activity of Cerium-Doped Bioactive Glasses; ACS Biomaterials Science & Engineering 2022 8 (7), 2890-2898.

[4] Gates-Rector S D, Blanton T N; The Powder Diffraction File: A Quality Materials Characterization Database Powder Diffr. 34 (2019) 352–60. https://www.icdd.com/pdfsearch/.

P028: A FLEXIBLE ELECTROCHEMICAL PLATFORM FOR HEALTH STATUS MONITORING IN DIABETIC PATIENTS

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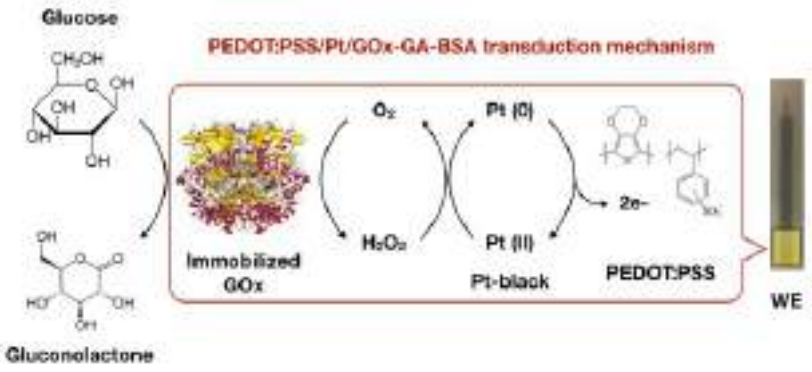
ABSTRACT

One of the main goals of scientific research regards taking care of people's health, therefore the need to monitor the body status for accurate and rapid management of critical health conditions has become a priority. Many electrochemical systems have been developed to monitor important biomarkers and the world of sensors for healthcare is wide. Scientific interest is moving nowadays towards the design of wearable and non-invasive devices for continuous and real-time monitoring, but many technological challenges are still unaddressed. The activity of our research group has recently focused on the development of flexible sensing platforms based on both OECTs (Organic ElectroChemical Transistors) and amperometric sensors configuration, fabricated by ink-jet printing technique. The matrix selected for the detection is the biofluid placed between cells and tissues called interstitial fluid (ISF), which reflects blood composition and might be non-invasively extracted through the skin without the use of needles, e.g. by reverse iontophoresis. The first step in designing the sensing platform concerned the development and optimization of a glucose sensor printed on a flexible plastic support. In particular, a soft material like the organic semiconductor PEDOT (poly(3,4-ethylenedioxy-thiophene)) doped with PSS (poly(styrene sulfonate)) was chosen as the electrochemical transducer and was then functionalized with platinum (Pt), the proper enzyme glucose oxidase (GOx) immobilized with a mixture of Bovin Serum Albumin (BSA) and Glutaraleyde (GA) in order to make the device sensible to glucose according to the reaction mechanism described in Figure 1. After evaluating performances and analytical parameters like repeatability and reproducibility, the following steps were focused on taking into consideration possible interference compounds, like lactate and paracetamol, and the evaluation of temperature's impact on the measurements.



PEDOT:PSS/Pt/GOx-GA-BSA functionalization

REFERENCES

[1] Teymourian H, Barfidokht A, Wang J. Electrochemical glucose sensors in diabetes management: An updated review (2010-2020). Chem Soc Rev. 2020;49(21):7671-7709. doi:10.1039/d0cs00304b
[2] Gualandi I, Tessarolo M, Mariani F, et al. Layered double hydroxide-modified organic electrochemical transistor for glucose and lactate biosensing. Sensors (Switzerland). 2020;20(12):1-15. doi:10.3390/s20123453
[3] Lai S, Casula G, Ricci PC, Cosseddu P, Bonfiglio A. All-organic, low voltage, transparent and compliant organic field-effect transistor fabricated by means of large-area, cost-effective techniques. Applied Sciences (Switzerland). 2020;10(19). doi:10.3390/APP10196656

P029: EFFECT OF COMPOSITION ON THE FUNCTIONAL PROPERTIES OF FULLY BIOBASED ALIPHATIC/AROMATIC POLYMERIC BLENDS

Alessandro Coatti[a], Mattia Manfroni[a], Elisa Boanini[b], Massimo Gazzano[b], Valentina Siracusa[c], Maddalena Negrin[d], Elena Macerata[d], Mario Mariani[d], Michelina Soccio[a], Nadia Lotti[a]

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ABSTRACT

Poly(butylene succinate) (PBS) is a biobased polymer that has attracted considerable interest in recent years due to its promising properties for a wide range of applications. It is a semicrystalline aliphatic polyester derived from succinic acid and butanediol, fully compostable and notable for its excellent processability, impact resistance and toughness [1]. On the other hand, PPeF is a relatively new biobased aromatic polyester, synthesized form dimethyl-2,5-furandicarboxylate and pentanediol; it is a rubbery polymer (with a glass transition temperature slightly below room temperature) with limited crystallization capability, showing excellent barrier properties [2]. Aiming to explore the evolution of solid-state properties across a range of compositions, a series of new PBS/PPeF blends was successfully developed and thoroughly characterized, building on the excellent performance previously reported for PBS/PPeF blends. To assess their suitability for flexible packaging applications, all materials were processed into films and tested for mechanical performance and permeability. Additionally, following a prior study [3], gamma radiation doses from 0 to 50 kGy were applied to both the original homopolyesters and the 50/50 blend to investigate the effects of sterilization on physicomechanical and thermal properties.

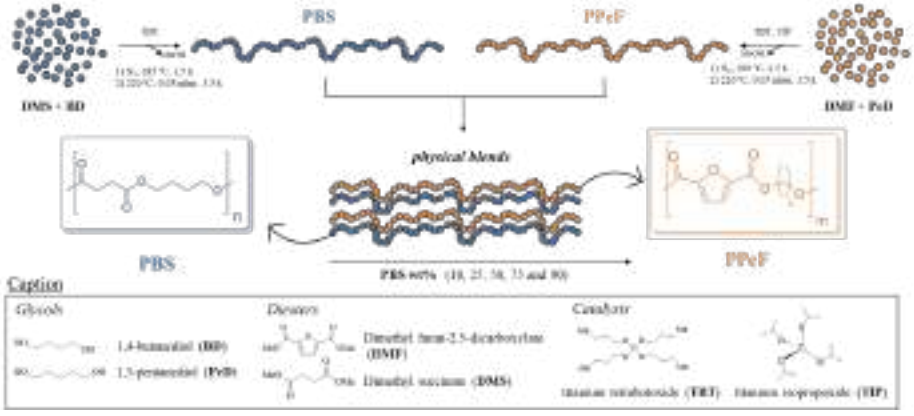

Figure 1. Reaction scheme

REFERENCES

[1] M. Barletta, C. Aversa, M. Ayyoob, A. Gisario, K. Hamad, M. Mehrpouya, H. Vahabi, *Prog. Polym. Sci.*, **2022**, 132, 101579.

[2] G. Guidotti, M. Soccio, M.C. Garcia-Gutierrez, E. Gutierrez-Fernandez, T.A. Ezquerra, V. Siracusa, A. Munari, N. Lotti, *ACS Sustain. Chem. Eng.,* **2019**, *7*, 17863-17871.

[3] M. Negrin, E. Macerata, G. Consolati, F. Quasso, L. Genovese, M. Soccio, M. Giola, N. Lotti, A. Munari, M. Mariani, Radiat. Phys. Chem., **2018**, 142, 34-43.

P030: Ru/Pd catalytic system for the reductive amination of furfural

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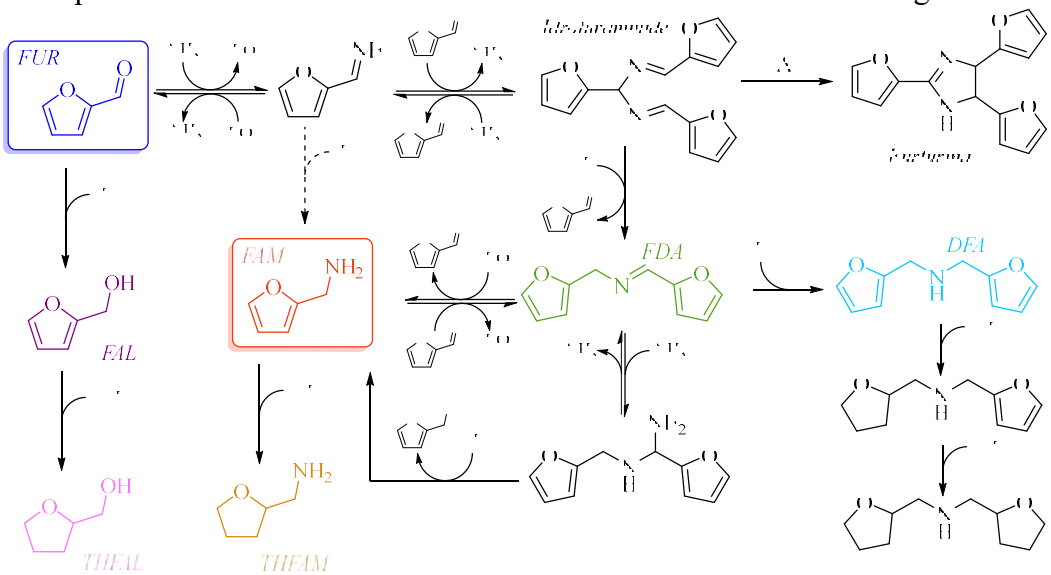
ABSTRACT

Introduction. In the last decades, supported metal nanoparticles (NPs) have been widely employed for the preparation of high-performance heterogeneous catalysts. Sol-immobilization is an efficient way for the synthesis of such catalysts, allowing the deposition of metal NPs, previously formed in an aqueous solution, on the support's surface[1]. The aim of the present work was to explore the preparation of some ruthenium-based catalytic systems supported on TiO2, also evaluating how the activity changes adding palladium in the active phase with various metal:metal ratio. The catalytic performances of the prepared solids have been evaluated in the reductive amination of furfural to furfurylamine.
Results. After an initial study of the influence of various reaction parameters, such as reaction time and temperature, H2 pressure and ammonia concentration, conducted on ruthenium catalyst, it was possible to identify optimized conditions that allowed achieving a selectivity for furfurylamine around 95%. The effect of various parameters and the results of reactions conducted without a catalyst were then used to delve into the intermediates involved in the process, an investigation that led to the hypothesis of a reaction scheme slightly different from the one usually proposed in the literature regarding the initial species formed (**Scheme 1**). Specifically, it was observed that in the first minutes of the reaction, a trimer of furfurylimine forms, which is then converted to N furfurylidenefurfurylamine (FDA) and, subsequently, to the primary amine of interest. Finally, to improve the reducing properties of the catalyst, bimetallic Ru/Pd catalysts were prepared, and with small amounts of palladium an improvement in catalytic activity was recorded. However, further increase in the palladium fraction leads to the reduction of the aromatic furan ring.



Scheme 1. *Proposed reaction scheme for the reductive amination of furfural (FUR) to furfurylamine (FAM).*

REFERENCES

[1] Monti, E.; Ventimiglia, A.; Forster, L,; Rodriguez-Aguado, E.; Cecilia, J.; Ospitali, F.; Tabanelli, T.; Albonetti, S.; Cavani, F.; Rivalta, I.; D'Agostino, C.; Dimitratos, N. *Green Chem.* **2023**, *25 (7)*, 2640-2652.

P031: NANOMEDICINE FOR RARE NEUROMETABOLIC DISEASES: BRIDGING THE LAB-TO-INDUSTRIAL GAP

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ABSTRACT

Enzyme replacement therapy (ERT) is promising for the treatment of rare neurometabolic diseases, including lysosomal storage disorders (LSD) like alpha-mannosidosis; however, the delivery of recombinant enzymes to the central nervous system (CNS) is still challenging. Despite the approval of Lamzede® (Velmanase alfa)[1] for the treatment of peripheral manifestations of alpha mannosidosis, the inability to target it to the CNS and issues related to intravenous administration, like immunogenicity and sensitivity to biological milieu, limit its therapeutic potential. Nanomedicine represents a potential solution to overcome the drawbacks of ERT, achieving brain delivery. This will pave the way for new therapeutic solutions with potential applications in other LSDs. In this view, a formulative protocol for the encapsulation of Lamzede®, in FDA-approved poly lactic-co-glycolic acid (PLGA) NPs, was optimized. Due to the high-cost of the marketed formulation, the enzyme β-glucosidase was used as a model. Although the double emulsion and solvent evaporation method (DE) formulative protocol was already optimized for β-glucosidase, in presence of stabilizers like Tween® and Bovine Serum Albumin (BSA)[2,3], the microfluidic (MF) technique was chosen for its versatility and ability to produce uniform and monodisperse NPs with minimal waste of solvents and reagents. Firstly, the optimization of the lab-scale MF protocol was evaluated varying the physical parameters of the syringe pump and the composition of NPs, including total flow rate, flow rate ratio, polymer concentration, enzyme to polymer ratio, type and concentration of surfactants and stabilizers. Once the protocol was optimized for the model enzyme, it was then adapted for the encapsulation of Lamzede® with minor modifications. Secondly, the MF protocol was translated to the industrial-scale using the automated nanoparticle system (ANP). Preliminary ANP results were similar to those obtained with the lab-scale instrument (∽300 nm, PDI<0.3, Z pot.<-30 mV) suggesting that a tunable and scalable nanoplatform was developed, offering a promising platform for enzyme delivery, which is readily scalable to industrial production. Preliminary data also confirmed the maintenance of enzymatic activity, while sophisticated *in vitro* models will provide valuable insights into the biological performance of the nanomedicines. All these results taken together set the stage for the transition of enzyme encapsulation from a bench top to an industrial production. Moreover, it will be possible to overcome other drawbacks of approved ERT therapies to achieve new and effective therapies for LSDs to close the gap between academia and industry. Moreover, the tunability and the possibility of targeting these NPs to the CNS hold promise to target a wide range of diseases, paving the way to new versatile therapeutic solutions.

REFERENCES

[1] *Lamzede® (velmanase alfa-tycv)* | *For patients and caregivers*. https://chiesi-lamzede-live.cphostaccess.com/ (accessed 2024-05-06).
[2] Duskey, J.T et al. *Molecules* **2020**, *25* (20), 4593. https://doi.org/10.3390/molecules25204593.
[3] Duskey, J.T et al. *Nanomaterials* **2021**, *11* (11), 2946. https://doi.org/10.3390/nano11112946.

P032: POLYANILINE-BASED MATERIALS FOR SMART BIOCOMPATIBLE NON-INVASIVE MEDICAL AND HUMIDITY SENSORS AND FLEXIBLE ALL-IN-ONE SUPERCAPACITORS

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ABSTRACT

Conductive polymers as polyaniline (PANI) can represent a simple and affordable answer to the necessity of flexible electronics. PANI in particular shows a peculiar doping/dedoping process, with high conductivity and tuneability, but lacks mechanically due to its fragility. However, different supports can enhance the mechanical properties of PANI, donating resilience, tenacity, and flexibility. The fabrication of different biocompatible devices based on PANI composite materials is here presented, respectively a paper-like sensor for humidity[1] and an all-in-one supercapacitor (SC).[2] PANI was polymerized with poly (2-acrylamido-2-methyl-1-propanesulfonic acid) (PAMPSA) for a more mechanically stable structure and enhanced conductivity, achieving PANI emeraldine state. Thus, when blended with cellulose fibres, the hygroscopicity of PANI provides a humidity-related conductivity increase. Consequentially, another interesting application as breath sensor and ECG was explored.[1] The application in energy storage field is then investigated with the insertion of PANI-PAMPSA in polyvinyl alcohol (PVA) hydrogel systems. PVA powder was dissolved in PANI-PAMPSA solution, inducing a physical crosslinking through freeze-thaw cycles and providing a self-healing ability to the device.[3] This all-in-one SC, completed with PVA-H_2SO_4 hydrogel interlayer and graphene-based electrodes, shows flexibility and durability, and it operates during and after physical deformation.[2]

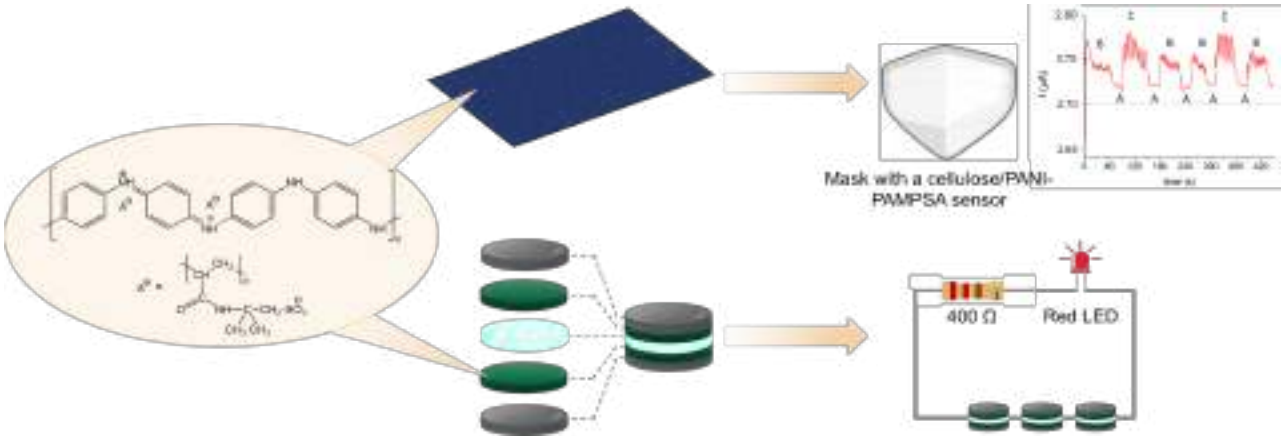

Figure 1. Chemical structure of PANI-PAMPSA and scheme of the observed applications

REFERENCES

[1] I. Ragazzini *et al.*, *Carbohydrate Polymers*, vol. 316, p. 121079, Sep. 2023.
[2] A. Giovagnoli, G. D'Altri *et al.*, *Gels*, vol. 10, no. 7, p. 458, Jul. 2024.
[3] G. D'Altri *et al.*, *ACS Omega*, vol. 9, no. 6, pp. 6391–6402, Feb. 2024.

P033: ELECTROSPUN FIBERS AS POTENTIAL REINFORCEMENTS FOR MEMBRANES USEFUL IN AEMWE APPLICATION

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ABSTRACT

Anion-exchange membrane water electrolysis (AEMWE) devices are electrochemical cells capable of performing water electrolysis in a basic environment, producing hydrogen and oxygen. They represent a crucial step in the hydrogen supply chain, as they enable the storage of electricity in the form of green fuel.[1] Within AEMWE cells, an ion-exchange resin ensures the ion transport necessary for the apparatus's operation. To improve the efficiency of these devices, the operating pressure can be increased; however, higher operating pressures may lead to damage to the ion-exchange resin. Therefore, enhancing the mechanical resistance of such membranes is of paramount importance.
A feasible approach involves integrating a nano- or microfibrous membrane, fabricated via electrospinning, to provide mechanical support and reinforcement to the "active" material, namely the ion-exchange resin.
This study aims to develop nanofibrous systems to mechanically support ion-exchange membranes. Different polymers, mainly fluorinated polymers [2], will be evaluated to obtain the best fibrous morphology and overall mechanical properties.[3]
The produced fibers have been characterized using SEM to correlate the morphology of the nanofibers with the various electrospinning parameters. Finally, after optimizing the solution and process, a membrane will be produced for subsequent integration tests with ion-exchange resins.

REFERENCES

[1] Li, D. *et al*.Durability of anion exchange membrane water electrolyzers. Energy and Environmental Science. 3393-3419 (2021)
[2] Belov, N. A., Alentiev, A. Y., Bogdanova, Y. G., Vdovichenko, A. Y. & Pashkevich, D. S. Direct Fluorination as Method of Improvement of Operational Properties of Polymeric Materials. Polymers (Basel). 12, 2836 (2020)
[3] Maccaferri, E. *et al.* Rubbery nanofibers by co-electrospinning of almost immiscible NBR and PCL blends. *Mater. Des.* 186, 108210 (2020)

P034: EVALUATING AMBERLITE RESINS FOR PFAS REMOVAL: A COMPARATIVE STUDY

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ABSTRACT

Per- and polyfluoroalkyl substances (PFAS) are synthetic chemicals known for their unique physicochemical properties and environmental persistence. Their widespread contamination and resistance to conventional degradation techniques pose significant challenges to water treatment. Granular activated carbon (GAC) is one of the most commonly used materials for PFAS adsorption due to its high surface area and established effectiveness in water treatment processes. However, GAC exhibits limited efficiency in removing short-chain PFAS, which are more mobile and less adsorbable, making them particularly challenging to address. This limitation underscores the need to explore alternative adsorbents capable of efficiently removing a broader range of PFAS compounds, including short-chain variants. In this study, we explored the adsorption performance of various resins, including XAD-4, XAD-7, L-493, and ROC-110, for the removal of PFAS from aqueous solutions. The adsorption capacities were determined using model PFAS compounds, such as perfluorooctanoic acid (PFOA), and compared with non-fluorinated organic acids, such as nonanoic acid, to assess selectivity. Analytical methodologies, including gas chromatography coupled with mass spectrometry (GC-MS) and liquid chromatography-mass spectrometry (LC-MS), were employed for quantifying PFAS adsorption. Fourier-transform infrared spectroscopy (FT-IR) provided further insights into the weak interactions between highly crosslinked resins and PFAS molecules. The study comprehensively evaluated the adsorption capacities of XAD-4, XAD-7, L-493, and ROC-110 resins, reflecting their distinct structural and compositional characteristics. Adsorption behavior was assessed across varying pH conditions, with neutral pH selected for capacity tests to simulate environmental scenarios. XAD-4 and L-493, both featuring a styrene-divinylbenzene framework, exhibited strong adsorption performance, benefiting from their high surface area and hydrophobic properties. The acrylic-based XAD-7 resin demonstrated the highest adsorption capacity, reaching approximately 26 mg/g, highlighting its superior performance under neutral conditions and its adaptability to pH variations. ROC-110, despite being a cation-exchange resin, contributed valuable insights into the role of resin chemistry in PFAS removal. Adsorption experiments revealed non-selective behavior across both perfluorinated and polyfluorinated compounds, emphasizing the broad applicability and versatility of these resins in water treatment. These findings suggest that macroreticular resins are promising candidates for PFAS remediation, adaptable to diverse environmental conditions and challenges. Regeneration tests demonstrated that a methanol-water mixture achieved an average PFAS recovery of 70% across all resins, surpassing other solvents tested, such as methanol alone or ammonium acetate. These results highlighted the regeneration capacity of macroreticular resins, which needs to be directly compared with that of GAC in future tests to assess their effectiveness under challenging conditions, such as high PFAS concentrations (100 ppm). This work highlights the importance of developing efficient and sustainable materials to address the environmental and health challenges posed by PFAS contamination, contributing to more effective water remediation strategies.

P035: CARBON NANOTUBES AS HYPERTHERMIA AGENTS IN REGENERATIVE MEDICINE

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ABSTRACT

The local delivery of a low heat dose can be exploited in regenerative medicine, augmenting tissue regeneration. Carbon Nanotubes (CNTs) efficiently convert near infrared radiation (NIR) into heat and are under extensive investigation because of their potential as intracellular nanoheaters [1]. However, the use of CNTs in biological systems still presents important restrictions due to 1) low biocompatibility; 2) dependency of their properties and toxicity on the physiological environment and 3) the related aggregation phenomena. Proteins can be used to disperse efficiently in water CNTs with a "green" supramolecular approach, minimizing undesirable toxic responses and controlling their biodistribution/cellular uptake [2]. Here we synthesized various CNT-protein hybrids using lysozyme and bovine serum albumin as model proteins and different CNTs (CNT(6,5) or CoMoCAT). The protein platform offered different chemical groups for an easy route of functionalization of the hybrids (figure 1), that were engineered by cationization (using cationizing agents such as ethylenediamine), or covalently linking targeting agents (i.e. EGF protein) and/or fluorescent tags (i.e. Fluorescein isothiocyanate) [3].

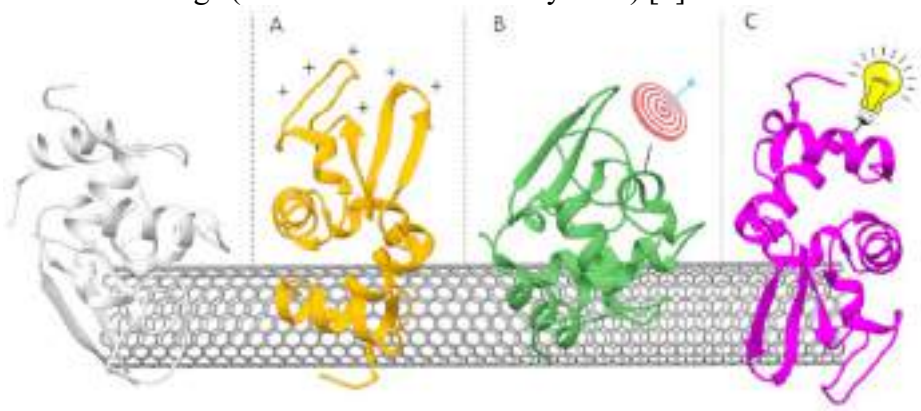

Figure 1. Engineering of CNT-Protein hybrids by cationization (A), bioconjugation of targeting agents (B) or fluorescent tags (C)

The stability of the nano-hybrids in different media was assessed, and their heating ability was measured upon NIR-irradiation. *Hydra vulgaris* was used as in vivo model, due to its capability of regenerate the complete individual from amputated body parts, to demonstrate the efficacy of the nanoplatform in regenerative medicine.

REFERENCES

[1] R. Singh, S. V. Torti, *Advanced Drug Delivery Reviews. 65* (2013) 2045-2060
[2] M. Calvaresi, F. Zerbetto, *Acc. Chem. Res. 46* (2013) 2454-2463
[3] M. Di Giosia, F. Valle, A. Cantelli, A. Bottoni, F. Zerbetto, E. Fasoli and M. Calvaresi, *Carbon*. 147 (2019) 70-82

ACKNOWLEDGMENT

Funded by the European Union – NextGenerationEU, Phoenix: Enhancing tissue regeneration through carbon nanoheaters, P2022LE4BE, CUP B53D23031710001.

P036: CYCLODEXTRIN-NOVEL CHAPERONE COMPLEXES FOR RETINAL DRUG DELIVERY: A PRELIMINARY STUDY

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ABSTRACT

Mutations in the rhodopsin gene (*RHO*) are the main cause of autosomal dominant retinitis pigmentosa (adRP). One of the most studied mutations is the P23H substitution resulting in RHO misfolding, endoplasmic reticulum retention, and rod degeneration leading to impaired visual function[1]. Pharmacological chaperones are small molecules that can bind misfolded RHO and promote its correct folding, representing a potential therapeutic approach. 13-*cis*-5,8 -epoxy retinoic acid (13-*cis*-5,8-ERA) has been identified as an effective chaperon for RHO mutations and a promising therapeutic agent for P23H-linked adRP[2]. Current retinal-targeted treatments rely on invasive methods (i.e. intravitreal injections) therefore development of less invasive delivery routes, such as eye-drops, is needed. Cyclodextrins (CDs) offer a potential alternative forming host-guest complexes with hydrophobic molecules, enhancing drug solubility, stability, and permeation through the ocular barriers[3]. In this view, an eye-drop formulation based on 2-Hydroxypropyl β-cyclodextrins (HPβCD), approved for ocular delivery, and 13-*cis*-5,8-ERA host-guest complexes could offer new therapeutic solutions for RHO misfolding mutations causing adRP.

Due to the high-cost of 13-*cis*-5,8-ERA, preliminary studies were performed with a similar-structured retinoid, 13-cis-retinoic acid (13-*cis*-RA). First, phase-solubility studies[4] were performed. The literature reports an 8-day requirement[5] for host-guest complex formation; 13-*cis*-RA quantification was performed after 4- and 8-days to reduce the formulation time. No significant differences were observed resulting in type Ap diagram for both time-points, suggesting a 1:2 (drug:cyclodextrin) molar ratio in line with estimations from molecular modeling of the 13-*cis*-5,8-ERA in complex with α-cyclodestrins. Complex formation was also assessed with DSC and Raman analyses. Preliminary ultra-high-performance liquid chromatography high-resolution mass spectrometry (UHPLC–HRMS) analyses were performed aiming to optimize a translatable analytical method that will work for the quantification of 13-*cis*-5,8-ERA in the retina.

These preliminary results set the stage for the stability constant evaluation and for the transition from 13-*cis*-RA to 13-*cis*-5,8-ERA, which has already shown neuroprotective effects after intravitreal administration in *Rho*$^{P23H/+}$ mice model. Since host-guest complexes have been formulated in Sorensen's phosphate buffer modified for ocular application (isotonic, pH 7.4), future experiments will focus on chaperone complexation and *in vivo* administration in order to assess PK of drug delivery to the retina and biological effects. An eye-drop solution based on these host-guest complexes will offer a non-invasive self-administrable and easy to use therapeutic option for P23H-linked adRP, improving patient quality life and compliance while reducing healthcare costs.

REFERENCES

[1] Nair et al. *Cureus***2024**, *16* (8), e66814. https://doi.org/10.7759/cureus.66814.

[2] Behnen et al. *iScience***2018**, *4*, 1. https://doi.org/10.1016/j.isci.2018.05.001.

[3] Loftsson et al. *Drug Deliv. Sci. Technol.***2007**, *17* (1), 3–9. https://doi.org/10.1016/S1773-2247(07)50001-8.

[4] Higuchi, T.; Connors, A. Phase Solubility Techniques; 1965.

[5] Yap, et al. *Eur. J. Pharm. Sci.***2005**, *25* (1), 49–56. https://doi.org/10.1016/j.ejps.2005.01.021.

P037: SINGLE TRICHOME PHYTOCANNABINOMICS OF A MEDICINAL CANNABIS VARIETY

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ABSTRACT

A targeted and an untargeted metabolomics analysis applied to phytocannabinoids (phytocannabinomics [1]) was developed for the first time to study the content of a single isolated cannabis trichome. The primary active compounds in *Cannabis sativa* L. are phytocannabinoids, contained in a specific structure called the glandular trichome. These trichomes are small structures (1-10 μm) with a gland where secretory cells release cannabis-specific compounds, known as phytocannabinoids, along with terpenes that, unlike phytocannabinoids, are common in various plants within the plant kingdom. This study focused on a targeted and an untargeted analysis of the complete phytocannabinome in medicinal cannabis varieties (such as FM2), using an ultra-high-performance liquid chromatography system coupled with high-resolution Orbitrap mass spectrometry (UHPLC-HRMS). The analysis involved the use of a core-shell reverse-phase column with a gradient allowing the elution of over 30 phytocannabinoids, identified through known standards purchased or synthesized in the laboratory. Using a stereoscope, a single trichome was isolated by a thin needle (0.45x13mm). The trichome was then placed in a test tube and dissolved in ethanol and the resulting solution was directly injected in the HPLC system and analyzed using the previously developed method [2].

Figure 1. Close-up of cannabis trichomes.

The qualitative investigation of phytocannabinoids was conducted by comparing retention times, molecular ions, and fragmentation spectra, allowing for the identification of numerous phytocannabinoids by comparison with authentic standards analyzed under the same conditions. Furthermore, an untargeted metabolomics method was developed using the Compound Discoverer software and a custom workflow based on in-house library of over 500 phytocannabinoids. This software-assisted analysis enabled the putative identification of more than 60 phytocannabinoids.
For the first time, the phytocannabinome of a single isolated trichome is described, paving the way for evaluating potential phytocannabinoid variations within a single plant and providing valuable insights into the exact topology of phytocannabinoid biosynthesis.

REFERENCES

[1] Cerrato A, Citti C, Cannazza G, Capriotti AL, Cavaliere C, Grassi G, et al. Phytocannabinomics: Untargeted metabolomics as a tool for cannabis chemovar differentiation. Talanta 2021;230:122313.
[2] Cerrato A, Cannazza G, Cinzia C, et al. Analytical Methodologies for Lipidomics in Hemp Plant. In: Hsu F-F, editor. Mass Spectrometry-Based Lipidomics: Methods and Protocols, New York, NY: Springer US; 2021, p. 257–73.

This work was funded by Fondo Di Ateneo Per La Ricerca Anno 2024 (FAR2024PD), A.D06@FAR2024_DIP@05FA-CANNAZZA_FARDIP_2024.

P038: COMBINATION OF CHEMOMETRICS AND SPECTROSCOPY FOR THE RAPID QUANTIFICATION OF INDIGOTIN AND INDIRUBIN IN NATURAL INDIGO SAMPLES

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ABSTRACT

Indigo has historically been a key substance in textile dyeing [1]. Traditionally extracted from plants such as *Indigofera tinctoria*, *Isatis tinctoria* and *Persicaria tinctoria*, natural indigo consists of two main components: indigotin, which gives the characteristic blue colour, and indirubin, which gives a red-violet hue [2]. Commercial natural indigo typically contains around 85% calcium carbonate, with the remainder being organic matter [3]. The inorganic component presents a challenge for colour identification as it is insoluble in both water and most common organic solvents. In an industrial setting, it is crucial to have a cost-effective and rapid technique, easily integrated into quality control processes, that accurately measures both indigotin and indirubin to determine their ratio. Absorption spectroscopy technique is well suited to this application, but UV-visible absorption spectra of indigotin and indirubin, registered in dimethyl sulfoxide, show a significant overlap between the maximum of indigotin (≃ 610 nm) and indirubin (≃ 560 nm). Therefore, in this study we propose a chemometric approach for the simultaneous quantification of the two analytes starting from the absorption spectra of commercial indigo samples. As a fundamental and necessary preliminary step, an HPLC-PDA procedure has been developed to determine the exact concentration of indigotin and indirubin in industrially produced natural indigo samples. Dimethyl sulfoxide with the addition of hydrochloric acid was used as a solvent to promote the complete dissolution of the two analytes Separation of indirubin and indigotin was achieved using a reverse-phase C-18 column and a mobile phase consisting of water and acetonitrile. Spectroscopic investigation was performed analysing a large number of samples, consisting of 13 industrially produced indigo samples and 74 artificial samples prepared properly mixing indigotin and indirubin. In particular, the concentrations of indigotin and indirubin ranged from 0.3 to 14.6 ppm and from 0.1 to 2.8 ppm, respectively. The obtained spectra were then divided into training set (53 spectra) and test set (34 spectra) to build Partial Least Square (PLS) and Multivariate Curve Resolution (MCR) models. First derivative and mean centring have been used as preprocessing methods before performing PLS regression. Indigotin and indirubin solution concentration were set as variables and have been autoscaled. Two latent variables have been selected according with the RMSECV to build the PLS model, obtaining in both cases high R^2 values and low percentage errors. Indigotin has an R^2 of 0.991 and a percentage error of 4.26% with a RMSEP of 0.250 ppm. Indirubin shows a R^2 of 0.993 and a percentage error of 5.96% with a RMSEP of 0.061 ppm. In the case of MCR model, three components have been selected. Also in this case, the model showed excellent performances, being the average error associated to the prediction of indigotin and indirubin equal to 4.08% for and 6.68%, respectively. Additionally, the absorption spectra of pure indigotin and indirubin predicted by the MCR model are in good agreement with experimental ones, emphasising the effectiveness of the model to predict the concentrations of the analytes when they are present as a mixture.

REFERENCES

[1] N. Stasiak et al., Acta Pol. Pharm. 2014, 71, 215–221.
[2] C. Ahn et al., J. Korean Soc. Cloth. Text. 2013, 37, 827–836.
[3] E. Frignani et al., Life 2024, 14, 59.

P039: EXPLORING THE METABOLIC CONSEQUENCES OF PIN1 DEPLETION IN MAMMALIAN SKELETAL MUSCLE

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ABSTRACT

PIN1 is an enzyme that plays a role in energy homeostasis by regulating the function of phosphorylated protein. Its involvement in controlling the metabolic behaviour of muscle myofibers remains to be fully understood.[1] In this study, we explored the metabolic variation caused by PIN1 depletion in mammalian skeletal muscles using a murine model. A metabolomic analysis was performed on slow-twitch soleus (SO) and fast-twitch tibialis anterior (TA) muscles, from *Pin1* knock out (KO, N=9) and wild type (WT, N=9) mice. The analysis was performed using high-resolution magic angle spinning nuclear magnetic resonance (HR-MAS NMR) spectroscopy, directly on tissue samples, without pre-treatment.[2]
Multivariate statistical analysis highlighted significant metabolic differences between SO and TA muscles. SO samples were found to have higher levels of lipids, fumarate, succinate, glutamate and glutamine, while TA samples exhibited higher content of creatine, glucose, lactate and pyruvate. These findings align with the notion that slow-twitching SO muscles have an oxidative metabolism, while fast-twitching TA muscles are characterized by glycolytic metabolism.
In *Pin1* depleted muscles, we observed changes suggesting a shift of TA muscle toward a more oxidative metabolic profile, while the alteration in SO were more nuanced.

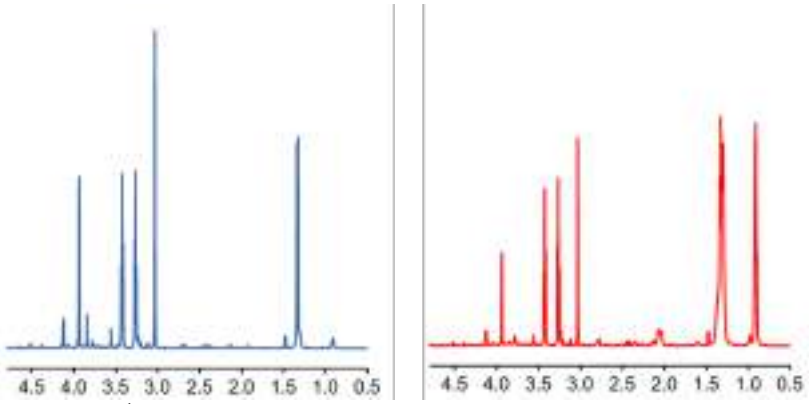

Figure 1: ^{1}H HR-MAS NMR spectra of TA (blue) and SO (red) muscles.

REFERENCES

[1] Y.C. Liou, X.Z. Zhou, K.P. Lu, Trends Biochem. Sci. 2017, 36, 501-514.
[2] L. Schenetti, A. Mucci, F. Parenti, R. Cagnoli, V. Righi, M.R. Tosi, V. Tugnoli, Concepts Magn. Reson. Part A 2006, 28A, 430-443.

P040: DESIGN AND SYNTHESIS OF HYDROPHOBIC TAG DEGRADERS FOR ANTIPARASITIC DRUG DISCOVERY AND CHEMICAL BIOLOGY APPLICATIONS

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ABSTRACT

Leishmaniasis, a vector-borne infection disease caused by protozoa of the *Leishmania* genus, is considered as an emerging and uncontrolled neglected tropical disease (NTD) by the World Health Organization. The recent climate change and migratory flows have increased the risk of exposure even in countries outside the endemic areas (mostly present in parts of the tropics, subtropics, and southern Europe). Unfortunately, existing treatments for leishmaniasis are still far from ideal, mainly due to an extensive toxicity, lack of efficacy, low patience compliance, prohibitive costs, increasing drug resistance and limited access to the cure.[1] Therefore, new and effective treatments are urgently needed. Targeted Protein Degradation (TPD) based on the paradigm of an event-*driven pharmacology*, could provide a promising solution.[2] TPD involves developing degraders that induce the degradation of the target protein through the activation of the proteasome system, rather than the typical occupation-*driven pharmacology* provided by conventional small molecule inhibitors.[3] This project focuses on the design and synthesis of small molecule degraders based on Hydrophobic Tags (HyTs) directed to the Trypanothione Reductase (TR). TR has emerged as a promising target for leishmaniasis, being essential for parasite survival and absent in the host. However, its large and featureless active site makes it difficult to target with traditional small molecules.[4] On this basis, HyTs may overcome these limitations. To design HyTs-directed TR, a ligand for TR has been selected, which will be combined via a linker with different hydrophobic moieties responsible for recruiting the degradation system.[5]
Overall, HyT-mediated TR degradation for leishmaniasis may lead to the development of a next-generation as antiparasitic drugs.

Figure 1. a) conventional small molecule inhibitors and degraders; b) chemical structures of some representative hydrophobic moieties.

REFERENCES

[1] Pinheiro, A. C. et al. *RSC Med. Chem.* **2022**, *13*, 1029–1043.
[2] Espinoza-Chávez RM. et al. *ACS Bio Med Chem Au*. **2022**, *3*, 32-45.
[3] Salerno, A. et al. *J. Med. Chem.* **2022**, *65*, 9507-9530.
[4] Battista, T. et al. *Molecules* **2020**, 25, 1924.
[5] He Q, Zhao X, Wu D. et al. *Eur J Med Chem*. **2023**, *260*, 115741.

P041: INFLUENCE OF ELECTROLYTE SOLUTION COMPOSITION ON PEDOT:PSS-BASED ELECTROLYTE-GATED TRANSISTORS

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ABSTRACT

Compared to the inorganic materials, conducting polymers (CPs) improve mechanical match when interfaced with tissue and establish low-impedance contacts due to their mixed electronic/ionic conduction which yield high effective capacitance. [1] Among the different CPs, the state-of-the art material for bioelectronic applications is poly(3,4-ethylenedioxythiophene) doped with poly(styrene sulfonate) (PEDOT:PSS). PEDOT:PSS has been successfully demonstrated as active material in Electrolyte-Gated Organic Transistor (EGOT) for biosensor [2] and *in-vivo* amplification of electrophysiological signal [3]. To achieve high performance, pristine PEDOT:PSS usually requires additives and chemo-physical post-treatments to improve its conductivity and stability. [4] Among these strategies, a great attention has been placed on the influence of PEDOT:PSS solution pH during film-cast fabrication. [5] However, no studies delved into the chemo-physical details of the influence of the electrolyte pH when PEDOT:PSS is used as active material in EGOTs. In this study, we systematically investigate how pH and ionic radius of cations in the electrolyte modify the electronic properties of a side-gated EGOT, in which PEDOT:PSS acts both as channel material and as Gate material. This study presents a unique correlation between the electrical performance variations observed in PEDOT:PSS-based EGOTs upon interaction of the active material with ions and protons (at different concentrations). Increasing the pH of electrolyte solution up to 11, we observe a decreasing of EGOTs channel current (I_{DS}) exceeding 40%, when compared to acidic electrolyte solution.

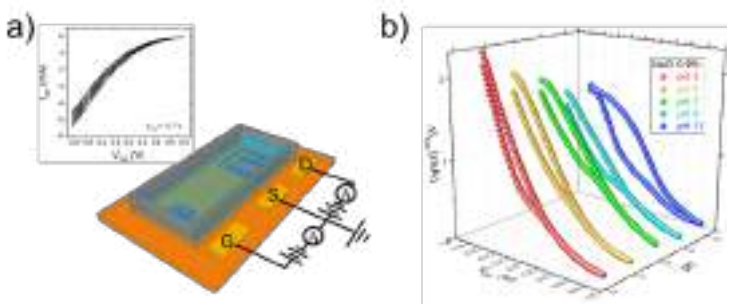

Figure 3: a) architecture of sided-gate EGOT b) normalized response at different pHs

REFERENCES

[1] J. Rivnay, R.M. Owens, G.G. Malliaras, The Rise of Organic Bioelectronics, Chem. Mater. 26 (2014) 679–685.
[2] M. Sensi, G. Migatti, V. Beni, T.M. D'Alvise, T. Weil, M. Berto, P. Greco, C. Imbriano, F. Biscarini, C.A. Bortolotti, Macromol. Mater. Eng. 307 (2022).
[3] M. Di Lauro, E. Zucchini, A. De Salvo, E. Delfino, M. Bianchi, M. Murgia, S. Carli, F. Biscarini, L. Fadiga, Adv. Mater. Interfaces. 9 (2022).
[4] C. Duc, A. Vlandas, G.G. Malliaras, V. Senez, Wettability of PEDOT:PSS films, Soft Matter. 12 (2016).
[5] J. Ouyang, Q. Xu, C.W. Chu, Y. Yang, G. Li, J. Shinar, On the mechanism of conductivity enhancement in poly(3,4- ethylenedioxythiophene):poly(styrene sulfonate) film through solvent treatment, Polymer (Guildf). 45 (2004).
[6] F. Kong, C. Liu, H. Song, J. Xu, Y. Huang, H. Zhu, J. Wang, Effect of solution pH value on thermoelectric performance of free-standing PEDOT:PSS films, Synth. Met. 185–186 (2013).

P042: CHARACTERISATION OF NOVEL PIN1 INHIBITORS AS POTENTIAL ANTICANCER AGENTS BY UHPLC-MS

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ABSTRACT

Elevated levels of prolyl-isomerase PIN1 enzyme have been implicated in a variety of aggressive cancers, and it has been shown to modulate critical signaling pathways related to tumor growth, metastasis, and chemotherapy resistance [1]. The primary goal of our multidisciplinary project is to test synthetic analogues of all-trans retinoic acid (ATRA, Fig.1) as potential PIN1 inhibitors and evaluate their efficacy, as well as their metabolism and stability.

From the analytical point of view, an original instrumental methodology based on ultra-high performance liquid chromatography coupled to mass spectrometry (UHPLC-MS) has been developed for the simultaneous analysis of ATRA and the synthetic analogues object of this project. Method validation on standard mixtures yielded good results in terms of linearity (6-500 ng/mL, $R^2 \geq 0.9991$), sensitivity (LOQ = 6 ng/mL), precision (RSD% < 1.3) and accuracy (RE% < 3.4). These results demonstrate the satisfactory sensitivity, precision and accuracy of the method, making it suitable for the analysis of ATRA and its analogues. This preliminary investigation is crucial in order to define the best experimental conditions to be applied during the following biochemical and metabolic studies, which are critical for assessing the pharmacological potential of new drug candidates.

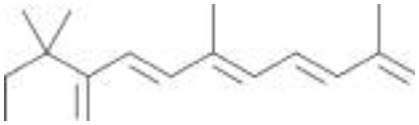

Figure 1. All-trans retinoic acid (ATRA)

In the following study step, advanced and miniaturised sample pretreatment protocols will be developed in order to be applied to complex samples. The pretreatment techniques currently under development are represented by miniaturised solid-phase extraction variants, namely stop-and-go extraction (StAGE) and microextraction by packed sorbent (MEPS). These protocols are being designed to optimize the reliable quantitation of the target compounds while reducing sample volumes, solvent usage and waste production [2].

This analytical study will be pivotal for the development of stable and effective PIN1 inhibitors that can be tested in subsequent stages of the project. The data obtained will guide the selection of the most promising compounds for further biological evaluation, ensuring that the final drug candidates are both effective and reliable in therapeutic settings.

This research was supported by National Recovery and Resilience Plan (PNRR), Mission 4 Component 2 Investment 1.1 – PRIN 2022 PNRR of the Italian Ministry of University and Research with European Union – NextGenerationEU funds, Project *PRIN-UNO* (P2022ZWY8H).

REFERENCES

[1] Campaner E, et al., Nat. Commun. 8 (2017) 15772.

[2] Protti M, et al., J Pharm Biomed Anal. 236 (2023) 115757.

P043: BIO-BASED FUNCTIONAL COATINGS DEVELOPMENT FOR SUSTAINABLE CELLULOSE PACKAGING

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ABSTRACT

The replacement of conventional packaging with sustainable alternatives that easily and safely degrade is a vital solution to decrease the disposal of plastic waste in landfills, rivers, and marine environments [1]. The biggest issue related to the use of fossil-based packaging is the end-of-life management. Waste disposal difficulties, and all the associated consequences are negatively affecting our lives. Cellulose, starch, chitosan, and polylactic acid can be considered promising alternative materials for conventional food packaging [2]. These biopolymers are eco-friendly, biodegradable, nontoxic, renewable, and biocompatible alternatives to synthetic packaging materials [3]. Many industries are revolutionizing their packaging practices and turning their focus to sustainability, driven by increasing consumer awareness and regulatory pressures. Among the various materials derived from renewable sources, cellulose is the most abundant natural organic compound widely present in plants and bacteria. Cellulose is also the agro-industrial waste that is most commonly reused [1]. Unfortunately, due to its porous structure and hydrophilic surface, natural cellulose substrates exhibit poor gas, moisture and liquid water barrier properties, wet strength, and antibacterial properties in high-humidity environments, which severely limits the application of cellulose paper products in high value-added applications such as food packaging [4]. Its use in this field can be realized only after a careful search for additives and green coatings to be introduced into the biopolymeric matrix to improve its thermal, mechanical, and barrier properties avoiding compromising recyclability and compostability of the final material. To address these needs, various methods, including chemical blending with hydrophobic coatings and strength additives, have been adopted to solve the aforementioned problems of natural cellulose substrates.
In the present project, linear and star-shaped molecules have been synthesized by esterification of fatty acids and polyols to create hydrophobizing treatments. The products have been characterized using spectroscopic and thermal analyses and then applied to pure cellulosic substrates. The product structures have been confirmed by ^{1}H-NMR and ATR spectroscopy. The melting (T_m) and degradation temperatures have been investigated using thermal analysis techniques such as DSC and TGA, which have shown T_m values ranging from 50°C to 70°C, depending on the nature of the product. SEM images have shown the formation of coatings with different morphologies depending on the shape of the molecules applied. As expected, water contact angle (WCA) measurements and Cobb tests have highlighted that the products obtained from the esterification of polyols and fatty acids with longer chain lengths impart higher hydrophobicity to the cellulose surfaces. To further improve the water repellency of cellulosic substrates, the combined effect of the synthesized products with an inorganic compound has been investigated on treated and dried samples. The presence of the inorganic compound has demonstrated an increased hydrophobic effect on the hydrophilic cellulose surfaces. SEM images have shown that after the combined application of the inorganic compound with the additives, each fiber is completely covered with a rough layer, which explains the increased WCA values and the improved water repellency.

REFERENCES

[1] F.Cirisano, M. Ferrari, Coatings, 11; 1508 (2021)
[2] Kumari S.V.G., Pakshirajan K., Pugazhenthi G., Int. J. of Biological Macromolecules, 221, 163-182 (2022)
[3] K.Y.Perera; A.K. Jaiswal; S. Jaiswal. Foods, 12, 2422 (2023)
[4] Huang H., Mao L., Wang W., Li Z., Qin C., International Journal of Biological Macromoecules, 236, 123630 (2023)

P044: PILLARED LIGAND MOFS WITH HYDROGEN BONDING SITES: FROM FLEXIBILIY TO APPLICATION

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ABSTRACT

Metal-Organic Frameworks (MOFs) are a class of highly porous materials composed of metal ions or clusters coordinated to organic ligands, forming a three-dimensional network. These materials are notable for their exceptional surface areas, tunable pore sizes, and structural versatility, which make them attractive for a wide range of applications, including gas storage, separation, catalysis, and sensing[1]. Among these materials, the use of the so-called "pillared" ligand metal-organic frameworks (PL-MOFs) has gained interest due to the possibility of using multiple ligands that can be conveniently functionalized to introduce anchoring points essential for host-guest chemistry[2]. In this presentation, we provide an insight into the engineering of some PL-MOFs, derived from the combination of three bis-amidic-bis-pyridinic ligands, differentiated by their rigid aromatic scaffolds, with three commonly used dicarboxylic acids: 4,4'-biphenyl dicarboxylic acid, 2,6-naphthalene dicarboxylic acid, and 1,4-benzenedicarboxylic acid.
The functionalization of the ligands with amidic moieties is essential for decorating the internal cavities of the MOFs with hydrogen bond (HB) donor and acceptor groups, which are crucial for the internalization of guest molecules. Furthermore, the use of pyridinic ligands, along with the introduction of conformationally free amide groups, imparts some degree of flexibility to the structure[3]. This flexibility can lead to the creation of flexible MOFs that exhibit interesting and diverse properties compared to more rigid compounds.
From these perspectives, the PL-MOFs described above will be analyzed in terms of their flexibility and dynamic behavior, focusing on their applications in host-guest chemistry, response to external stimuli, and gas sorption properties.

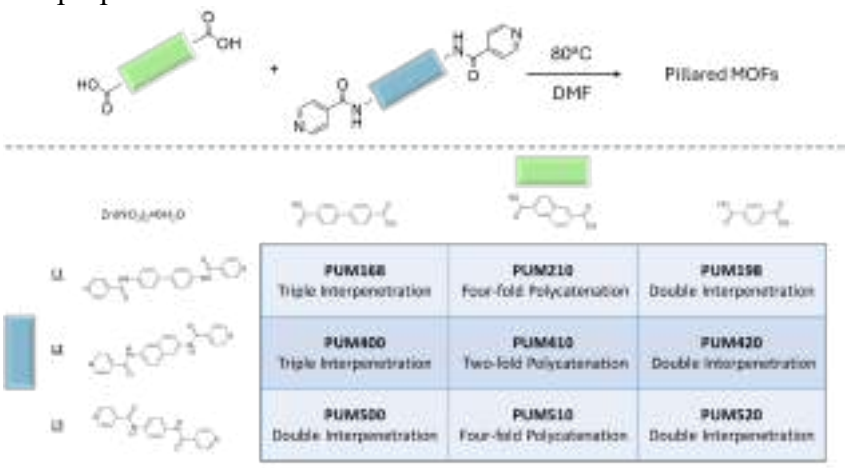

Figure 1. Schematization of the synthesized PL-MOFs

REFERENCES

[1] D. Li, A. Yadav, H. Zhou, K. Roy, P. Thanasekaran and C. Lee, Global Challenges, 2023
[2] M. Kondo, T. Okubo, A. Asami, S.H. Noro, T. Yoshimoto, S. Kitagawa, T. Ishii, H. Matsuzaka, K. Seki, Angewandte Chemie, 1999
[3] C.R. Murdock, B.C. Hughes, Z. Lu, D.M. Jerkins, Coordination Chemistry reviews, 2013

P045: USE OF AN URSODEOXYCHOLIC ACID-CONJUGATED OLIGONUCLEOTIDE FOR IN VITRO STUDIES OF INTESTINAL PERMEATION FOR THE TREATMENT OF DUCHENNE MUSCULAR DYSTROPHY

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ABSTRACT

Delivery represents one of the major hurdles to the clinical advancement of oligonucleotide therapeutics, especially in the treatment of a genetic disorder such as Duchenne muscular dystrophy (DMD). [1]

In this preliminary study, we explored the ability of 2′-O-methyl-phosphorothioate antisense oligonucleotides (ASOs) conjugated with a lipophilic molecule, such as ursodeoxycholic acid (UDCA), to permeate across intestinal barriers in vitro by a co-culture system of non-contacting IEC-6 cells and DMD myotubes, either alone or encapsulated in exosomes.

Ursodeoxycholic acid was employed to enhance the lipophilicity and membrane permeability of ASOs, aiming to potentially improve oral bioavailability. [2,3] Exosomes, instead, were used for their high biocompatibility and ability to deliver therapeutic cargo across biological barriers.

Exon skipping was evaluated in the DMD myotubes to reveal the targeting efficiency. Exosomes extracted from milk and wild-type myotubes loaded with 5′-UDC-3′Cy3-ASO 51 and seeded directly on DMD myotubes appear able to fuse to myotubes and induce exon skipping, up to ~20%.

Permeation studies using the co-culture system were performed with 5′-UDC-3′Cy3-ASO 51 alone or loaded in milk-derived exosomes. However, in this setting, only gymnotic delivery induced significant levels of exon skipping (almost 30%) suggesting a possible role of the intestinal cells in enhancing delivery of ASOs.

These results warrant further investigations to elucidate the delivery of ASOs by gymnosis or exosomes.

REFERENCES

[1] Takeda, S.; Clemens, P.R.; Hoffman, E.P. Exon-Skipping in Duchenne Muscular Dystrophy. J. Neuromuscul. Dis. **2021**, 8, S343–S358.

[2] Wang, S.; Allen, N.; Prakash, T.P.; Liang, X.; Crooke, S.T. Lipid Conjugates Enhance Endosomal Release of Antisense Oligonucleotides into Cells. Nucleic Acid Ther. **2019**, 29, 245–255.

[3] Marchesi, E.; Cortesi, R.; Preti, L.; Rimessi, P.; Sguizzato, M.; Bovolenta, M.; Perrone, D. Antisense Oligonucleotides Conjugated with Lipophilic Compounds: Synthesis and In Vitro Evaluation of Exon Skipping in Duchenne Muscular Dystrophy. Int. J. Mol. Sci. **2022**, 23, 4270.

P046: EXPLORATORY ANALYSIS OF MEDICINAL CANNABIS OILS PREPARATIONS PRODUCED IN BRAZIL

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ABSTRACT

Medicinal cannabis products represent an alternative therapeutic strategy for addressing various diseases. One example is refractory epilepsy, which mainly affects children. Research has shown that the use of cannabidiol (CBD) reduces seizure episodes. Legalized cannabis products are expensive, leading to an increase in the production of artisan cannabis preparations by patients' families and non-profit associations in Brazil. Since these products are not regulated by the national health authority, their cannabinoid content must be analyzed to ensure the intended therapeutic effect. Samples of cannabis oils produced by associations were analyzed by HPLC-DAD (28), using a modificatied method based on Carvalho [1]. For quality assessment, five cannabinoids were quantified (CBDA, cannabidiolic acid; THCA, tetrahydrocannabinolic acid; CBD, cannabidiol; THC, tetrahydrocannabinol; and CBN, cannabinol). Figure 1a shows a chromatogram of a multicomponent standard, prepared with these five cannabinoids. About half of the samples (15) provided label information on the content of CBD, THC, or their mixtures. In the oils, the presence of other cannabinoids can provide information about the quality. For example, the presence of CBN indicates THC degradation, while the presence of the acidic forms (CBDA and THCA) suggests that decarboxylation of the plant material was inadequate. An exploratory analysis using principal component analysis (PCA) was performed with the entire chromatogram data, where the peaks were aligned, making it possible to differentiate the samples according to the type and concentration of the main cannabinoids, THC, and CBD (Figure 1b). None of the samples analyzed, however, contained the same percentage of THC and/or CBD as declared on the label. All showed a significantly different THC/CBD content, ranging from 0.3% to 145% of the declared content. Some of the samples showed levels of CBN, THCA, and CBDA, with maximum concentrations of 0.25%, 2.21%, and 1.71%, respectively. According to reports from associations about the production of medicinal cannabis oils, often the quantity declared on the label refers to the crude extract of the plant, not the specified cannabinoids (CBD or THC). Although *Cannabis ssp*. is not yet considered a medicinal plant in Brazil, the correct way to label medicinal cannabis oils, due to their preparation method, would be the same as standardized herbal products. These labels should indicate the percentage of both the crude extract and the CBD or THC contained in these extracts

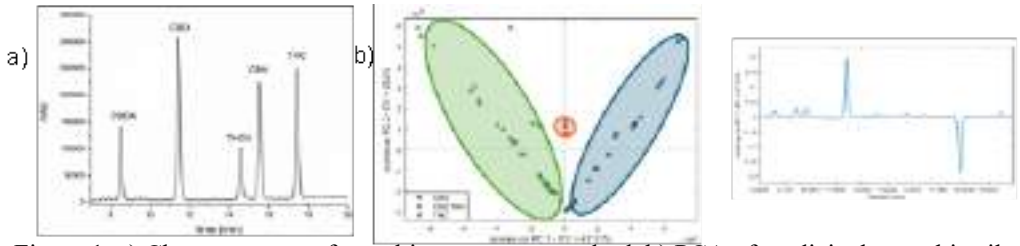

Figure 1. Figura 1. a) Chromatogram of a multicomponent standard. b) PCA of medicinal cannabis oils (scores and loadings plots).

REFERENCES

[1] T Carvalho, V.; Aguilar, A.; Baratto, L.; Souza, F.; Rocha, E.; Quim. Nova, 43, 2020, 90.

P047: MODELING PEPTIDE-GPCR-G PROTEIN COMPLEXES USING ALPHAFOLD 2 AND CLASSICAL MOLECULAR DYNAMICS: THE HNPS-NPSR-GQ CASE STUDY

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ABSTRACT

Neuropeptide S (NPS) is a 20-residue peptide that, through the activation of the Gq/Gs coupled NPS receptor (NPSR), regulates important physiological functions involved in anxiety, food intake, and locomotor activity[2]. Despite the extensive amount of data available on the endogenous peptide ligand, an experimental structure of the NPS-NPSR complex is not available yet thus hindering structure-based drug design efforts. To address this challenge, we generated a model of the NPS-NPSR-Gαq complex, by leveraging an AlphaFold2-based protocol which previously allowed us to predict another peptidergic complex structure with high accuracy[1]. The model was subjected to classical molecular dynamics (MD) simulations, that confirmed its stability and consistency with known structure-activity relationships. Through an in-depth model analysis, we identified key structural features essential for receptor activation and were able to retrospectively validate the pharmacological activities of known NPSR peptide ligands. We believe that this work represents a significant step towards understanding the NPS-NPSR interaction and paves the way for the development of new small-molecule and peptide ligands targeting this neuro-peptidergic system.

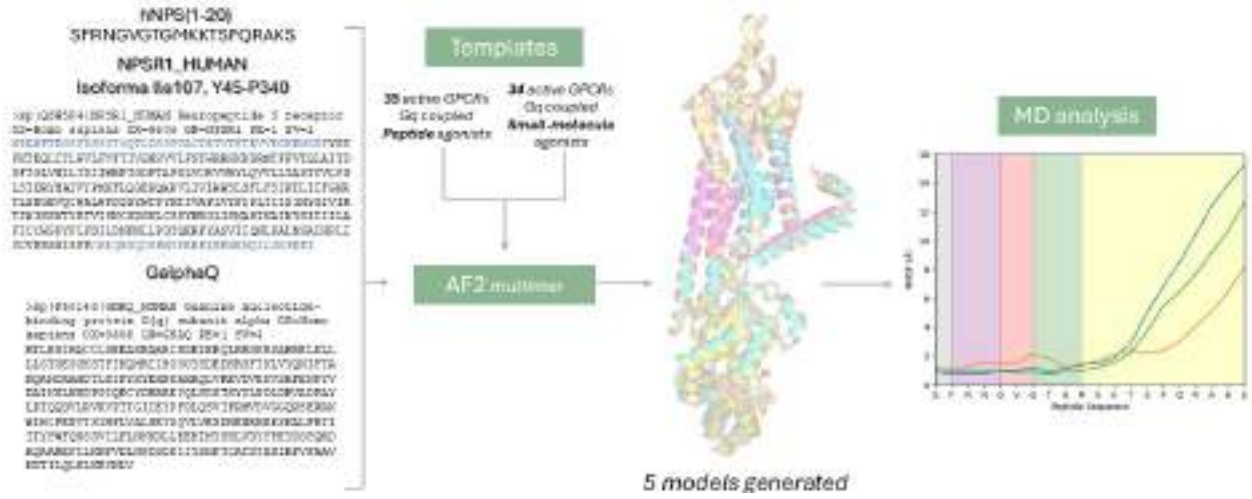

Figura 2 Workflow of the model generation

REFERENCES

[1] Ciancetta, A.; Malfacini, D.; Gozzi, M.; Marzola, E.; Camilotto, R.; Calò, G.; Guerrini, R. A Multi-Angle Approach to Predict Peptide-GPCR Complexes: The N/OFQ-NOP System as a Successful AlphaFold Application Case Study. *J. Chem. Inf. Model.* **2024**. https://doi.org/10.1021/acs.jcim.4c00499.
[2] Guerrini, R.; Salvadori, S.; Rizzi, A.; Regoli, D.; Calo', G. Neurobiology, Pharmacology, and Medicinal Chemistry of Neuropeptide S and Its Receptor. *Med Res Rev* **2010**, *30* (5), 751–777. https://doi.org/10.1002/med.20180.

P048: DEVELOPMENT OF DUAL FLT3-RET INHIBITORS FOR ACUTE MYELOID LEUKEMIA: IN SILICO DESIGN AND LIPOSOME-BASED DRUG DELIVERY

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ABSTRACT

Acute Myeloid Leukemia (AML) is a malignant cancer caused by the abnormal growth and differentiation of hematopoietic stem cells. FLT3 is a tyrosine kinase involved in the proliferation, differentiation, and apoptosis of hematopoietic cells and lymphocytes. Inhibition of mutated FLT3 has been proposed as a therapeutic strategy for the treatment of AML.[1,2] RET is another protein kinase identified as a co-factor for cellular activity in AML.[3] The main goal of this project is the creation of a library of dual inhibitors targeting RET and FLT3, designed in silico and characterized by the presence of a ureic scaffold. To enhance therapeutic efficacy and reduce toxicity, liposomes can be employed as controlled drug release systems.[4] The structures were designed in collaboration with Prof. Marzaro's research group at the University of Padua, and their biological rationale and profiling was carried out in collaboration with Prof. Mologni at the University of Milano Bicocca. The target compounds include a pyrazole and another polyaromatic group linked by a ureic linker; the polyaromatic group can consist of a biphenyl or two aromatic parts connected by a heteroatom, such as secondary anilines or phenolic ethers. It has been previously observed that the presence of a heteroatom bridge between the two rings influences the selectivity profile of the inhibitors, with biphenyl compounds being more selective for FLT3 and compounds with the heteroatomic linker showing a dual inhibition profile for both FLT3 and RET.

REFERENCES

[1] Yuan, T. *et al.* Dual FLT3 inhibitors: Against the drug resistance of acute myeloid leukemia in recent decade. *Eur J Med Chem* **178**, 468–483 (2019).10
[2] Pemmaraju, N., Kantarjian, H., Ravandi, F. & Cortes, J. FLT3 inhibitors in the treatment of acute myeloid leukemia. *Cancer* **117**, 3293–3304 (2011).
[3] Rudat, S. *et al.* RET-mediated autophagy suppression as targetable co-dependence in acute myeloid leukemia. *Leukemia 2018 32:10* **32**, 2189–2202 (2018).
[4] Liu, P., Chen, G. & Zhang, J. A Review of Liposomes as a Drug Delivery System: Current Status of Approved Products, Regulatory Environments, and Future Perspectives. *Molecules* vol. 27 Preprint at https://doi.org/10.3390/molecules27041372 (2022).

P049: METAL−HYDROXIDE ORGANIC FRAMEWORKS FOR ENERGY APPLICATIONS

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ABSTRACT

Modern society is deeply dependant on energy production for nearly all activities. While fossil fuels have long been the dominant energy source, their significant disadvantages are widely recognized. A promising alternative to tackle these challenges involves converting electricity into chemical energy through Electrochemical Water Splitting (EWS). This sustainable technique generates H_2, which can be stored or used as a clean energy alternative to fossil fuels [1]. However, EWS faces obstacles, in particular the high overpotential (+1.23 V) [1] needed for the 4-electron Oxygen Evolution Reaction (OER). To address these challenges, catalysts are indispensable; yet, commercial electrolyzers often rely on costly and rare elements like platinum, iridium, and ruthenium. An innovative approach to enhance the OER involves exploiting the Chiral Induced Spin Selectivity (CISS) effect. Using enantiomerically pure catalysts can enable spin-selective EWS, favoring the generation of triplet ground state O_2 (S = 1) while preventing the formation of singlet state (S = 0) by-products, such as hydrogen peroxide (H_2O_2). We chose to employ chiral Metal-Hydroxide Organic Frameworks (MHOFs) as spin-selective catalysts for the OER. In recent years, MHOFs have gained considerable attention as catalysts for EWS due to their remarkable properties, including high surface area, substantioal porosity, and well-defined structural organization. These materials feature a layered structure of metal hydroxides sheets intercalated with organic ligands (Fig. 1, A). Building on recent work of Yuan et al. [3], we initially synthetized $[M_2(OH)_2(BDC)]$, where M is Co^{2+} or Ni^{2+} and H_2BDC is terephthalic acid (Fig. 1, B). Subsequently, we modified H_2BDC introducing an alkoxy side chain, obtaining a chiral ligand and its achiral analogue: H_2BDCPe and H_2BDCBu (Fig. 1, D and C). Finally, these ligands were incorporated in two families of compounds, produced by either intercalation with $M(OH)_2$ or direct self-assembling from MBr_2. Cyclic Voltammetry measurements revealed that the chiral MHOFs indeed perform more effectively than their achiral counterparts. These results are promising and encourage further exploration of MHOFs and their role as catalysts for OER.

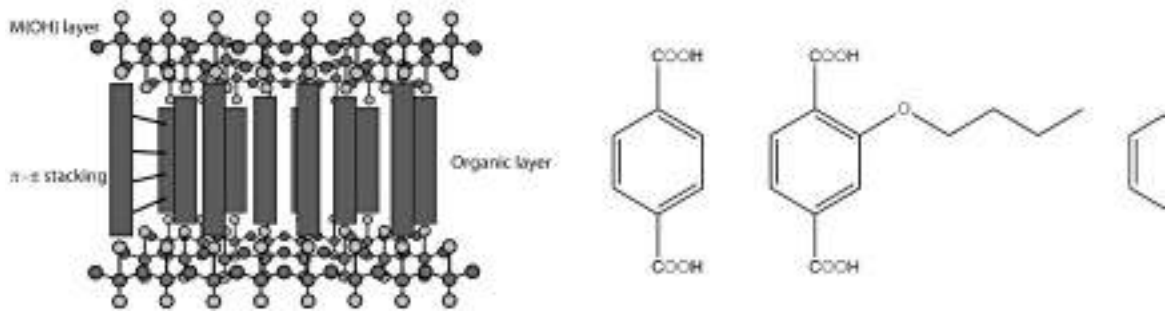

Figure 4. A: generic layred structure of a MHOF; B: H_2BDC; C: H_2BDCBu and D: H_2BDCPe.

REFERENCES

[1] Raveendran A, Chandran M, Dhanusuraman R., RSC Adv, 13 (2023), 3843-3876.
[2] Naaman et al., Science, 283 (1999), 814-816.
[3] Yuan et al., Nat. Mater., 21 (2022), 673-680.

P050: PHOTOELECTROCHEMICAL SOLAR HYDROGEN

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ABSTRACT

The research goal is to produce hydrogen from water by "water splitting" [1], using only sunlight to perform the redox reaction:

$$2H_2O + 4h^+ \rightarrow O_2 + 4H^+ \text{ (1.23V vs SHE, 25°C)}$$

$$4H^+ + 4e^- \rightarrow 2H_2 \text{ (0V vs SHE, 25°C)}$$

To carry out this process, we use a special device called PEC (Photoelectrochemical Cell), which can absorb solar light and convert it first into electrical energy and then into chemical energy stored in molecules (in this case, hydrogen). A photoelectrochemical cell consists of a working electrode (WE) that works with sunlight, a counter electrode (CE) where charges are transferred and a reference electrode (RE) to establish a controlled bias. However, the final industrial PEC will only consist of only the WE and CE. All these components are immersed in a conductive electrolyte and the cell performance is tested under solar illumination at standard conditions (0.1 W/cm^2, i.e. 1 sun), by measuring the photocurrent generated. The key element of PEC is the WE, which is usually a conductive substrate covered with a semiconductor, which is the light-harvesting material. Most of them are metal oxides, n-type semiconductors that can realize oxidation reactions under illumination which are used to construct the photoanode in the PEC. In this work, WO_3 and α-Fe_2O_3 (hematite), which are characterized by their ability to absorb light from the solar spectrum, non-toxicity and low cost, are used as metal oxide semiconductors for the photoanode. These materials are deposited on a titanium foil used as an ohmic collector by autoclave growth, following the solvothermal synthesis [2] for WO_3 and the hydrothermal synthesis [3] for α-Fe_2O_3. The challenge is to optimize these semiconductors in terms of film thickness, nanostructure morphology and light harvesting to achieve the best possible photocurrent necessary to reduce water to hydrogen. The choice of a metal substrate can be convenient because of its intrinsic conductivity and flexibility, since in the final PEC prototype the photoanode is curved to focus sunlight on the active area by a parabolic concentrator with linear focus. Both sides of the titanium foil are available for photoactive deposition and can be used simultaneously to generate photocurrent under solar irradiation. Another advantage of this technology is the possibility to perform an alternative reaction to oxygen evolution, using water which containing easily oxidizable organic pollutants [4,5]. These molecules allow to consume the hole, reducing the recombination process and maximizing the hydrogen production at the counter electrode.

REFERENCES

[1] A. Fujshima, K. Honda, Nature, 1972, 238, 37
[2] Grimes et al., Nano Lett. 2011, 11
[3] J. Deng et al., J. Appl. Phys., 112, 084312, 2012
[4] Cristino et al., *J. Mater. Chem. A*, 2016,4, 2995-3006
[5] Asif et al., Hematite-based nanomaterials for photocatalytic degradation of pharmaceuticals and personal care products (PPCPs): A short review, Current Opinion in Green and Sustainable Chemistry, Volume 28,2021,100447

P051: MORPHOLOGY OF ELASTOMERIC ELECTROSPUN MATS CONTAINING PLA

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ABSTRACT

Carbon Fiber Reinforced Polymer (CFRP) composite materials are currently used in all those fields where both excellent mechanical properties and low density are required, such as in the sports, automotive, aerospace and aviation industries. CFRPs, in fact, possess specific properties far superior to traditional materials such as steel, making it possible to obtain products with equal stiffness and strength, but much lighter. Still today, the widespread use of laminated composite materials is often limited by their low delamination resistance and low damping ability [1]. One possible solution to these problems consists in interleaving nano- or micro-fibrous mats within laminated composites [2] [3].
This experimental work aims to develop rubbery nanofiber nonwoven mats that could potentially enhance the delamination resistance and damping ability of epoxy-based CFRP laminates. In particular, the present work investigates the morphology of microfibrous fibers made of poly(lactic acid) (PLA) and rubber blends, obtained via electrospinning.
Stable solution blends were obtained, i.e., solutions that did not give rise to the phenomena of demixing/precipitation of one or both polymers. Specifically, the phenomenon of demixing depends on the rubber content in the blend and on the total polymer concentration. Solution blends containing a high amount of rubber with respect to the overall polymeric fraction were obtained and electrospun. The morphology analysis of the resulting mats was performed by SEM (Scanning Electron Microscope), confirming the possibility of obtaining fibrous membranes potentially useful for contrasting composites' delamination and, thus, extending the materials' durability.

REFERENCES

[1] Turon, A.; et al. A Damage Model for the Simulation of Delamination in Advanced Composites under Variable-Mode Loading. Mech. Mater. 2006.
[2] Palazzetti, R.; et al. Electrospun Nanofibers as Reinforcement for Composite Laminates Materials – A Review. Compos. Struct. 2017.
[3] Povolo, M.; et al. Damping and Mechanical Behaviour of Composite Laminates Interleaved with Rubbery Nanofibers. Compos. Struct. 2021.

P052: INTEGRATED EXPERIMENTAL AND THEORETICAL ANALYSIS OF THE HOMOGENEOUSLY CATALYZED GUERBET REACTION WITH RUTHENIUM-NHC COMPLEXES

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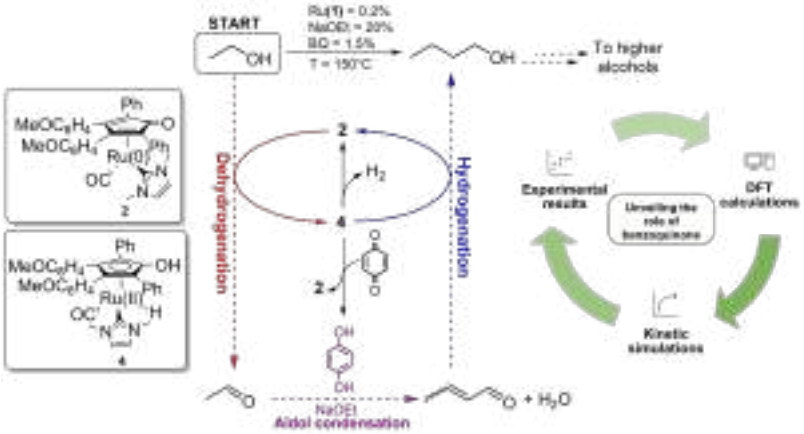
ABSTRACT

Benzoquinone has proven to be an effective co-catalyst in the ruthenium/NaOEt-catalyzed Guerbet reaction,[1-2] a process widely studied for converting bioethanol into higher-value chemicals like n-butanol.[3] The co-catalytic behavior of benzoquinone was explored through both experimental and computational approaches. Experimental findings showed substantial improvements in reaction performance, with a 25% increase in ethanol conversion, an 18% rise in higher alcohol yields, and a 13% reduction in molecular hydrogen byproduct formation. Density Functional Theory (DFT) calculations investigated two possible mechanisms to explain these kinetic effects: (i) a hydrogen storage mechanism and (ii) a basic co-catalysis via 4-hydroxyphenolate. The latter hypothesis showed the most promise, involving a mixed mechanism for the aldol condensation step in which hydroquinone (the reduced form of benzoquinone) acts as an alternative proton source to ethanol. This alternative mechanism proved to be more favorable than the aldol condensation occurring without any additive, indicating a positive impact on the overall reaction kinetics.



Scheme 1. Mechanistic insight on the role of benzoquinone in the Ru/NaOEt catalytic cycle

Various phenol derivatives were also tested as co-catalysts in the Guerbet reaction, with each showing improved process performance. This suggests that an aromatic acid stronger than ethanol could effectively enhance reaction kinetics. This hypothesis was further validated through theoretical kinetic simulations based on the DFT results, where the mixed mechanism closely matched experimental outcomes, reinforcing its role within the kinetic network of the reaction.

REFERENCES

[1] Mazzoni, R.; Cesari, C.; Zanotti, V.; Lucarelli, C.; Tabanelli, T.; Puzzo, F.; Passarini, F.; Neri, E.; Marani, G.; Prati, R.; Viganò, F.; Conversano, A.; Cavani, F. *ACS Sustain. Chem. Eng*. **2019**, *7*, 224.

[2] Cesari, C.; Gagliardi, A.; Messori, A.; Monti, N.; Zanotti, V.; Zacchini, S.; Rivalta, I.; Calcagno, F.; Lucarelli, C.; Tabanelli, T.; Cavani, F.; Mazzoni, R. *J. Catal.* **2022**, *405*, 47.

[3] Aitchison, H.; L. Wingad, R.; F. Wass, D. *ACS Catal.* **2016**, *6*, 7125.

P053: AMINO-ACID SUBSTITUTION CAN DEEPLY AFFECT THE ACTIVITY AND STABILITY OF ANTIMICROBIAL PEPTIDES

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ABSTRACT

Antibiotics are powerful life-saving drugs, but, in the last decades, they have been losing their effectiveness due to antimicrobial resistance (AMR), one of the major threats to global health. The excessive and inappropriate use of these drugs has sparked an evolutionary process within bacteria, resulting in the development of diverse resistance mechanisms. Nonetheless, all kingdoms of life are powerful sources of biomolecules possessing potential antimicrobial properties. Among these biomolecules, *cryptides* are particularly promising [1]. They are the results of the protein maturation processes, which lead to the formation of many peptides as "waste products"; they can display a wide range of bioactivities, such as host defense, protease inhibition, opioid, antithrombotic, signaling. Among *cryptides*, antimicrobial peptides (AMPs) are short peptides with a broad spectrum of activity. They are excellent candidates for the development of novel drugs due to their ability to act through diverse mechanisms of action (membrane disruption, inhibition of intracellular processes, biofilm demolition, and nutritional immunity) and their low susceptibility toward resistance phenomenon development. Depending on peptide sequence, some AMPs can sequester metal ions, which are fundamental for pathogen virulence (nutritional immunity). Furthermore, the metal-complex formation can enhance AMPs antimicrobial activity.
Calcitermin (VAIALKAAHYHTHKE), a very interesting antimicrobial peptide, is a 15 residues peptide, deriving from the C terminal domain of calgranulin C, a pro-inflammatory protein of the S100 family. It presents an effective metal binding domain corresponding to the three alternated histidine (His 9, His 11 and His 13) and the free terminal amino and carboxyl groups. Specifically, the coordination of metal ions, such as Cu^{2+} and Zn^{2+}, has the potential to enhance the antimicrobial activity against common bacteria, like *Staphylococcus aureus* and *Enterococcus faecalis* and against the fungi *Candida albicans* at acidic pH. During the past few years, our research group has undertaken a systematic study on calcitermin derivatives obtained by introducing modifications in the amino acid sequence of the native peptide, with the aim of studying their impact on the stability in plasma, metal coordination and antimicrobial activity of the peptide. We introduced some histidine-to-alanine substitutions [2], in order to evaluate the impact of alternated histidine in the metal binding domain. In addition, we studied alanine-to-serine substitutions in the proximity of the metal binding site [3], with the aim of favoring the coordination of amide nitrogens to the copper ion. Further modifications were alanine-to-histidine and alanine-to-arginine [4], in order to increase the overall net positive charge of the peptide, thus favoring the interaction with bacterial membranes. Cu^{2+} and Zn^{2+} have been investigated as metal ions. The characterization of the complexes has been achieved by means of potentiometry, UV-Vis spectrophotometry, circular dichroism, electron paramagnetic resonance and mass spectrometry. As for the peptide stability in human plasma, we focused on the degradation processes carried out by exo-peptidases by introducing terminal protections [5] or substituting L-amino acids at the terminal ends with the corresponding D-analogues. The evaluation of enzymatic stability has been achieved by HPLC.

REFERENCES

[1] Ueki N. *et al.,* Biopolymers **2007**, *88*(2), 190-198.
[2] Bellotti D. *et al.,*Dalton Transaction **2019**, *48* (36), 13740-13752.
[3] Leveraro S. *et al.,* Dalton Transaction, **2021**, *53*, 12676-12687.
[4] Leveraro S. *et al.,* Journal of Inorganic Biochemistry, **2025**, *262*, 112761.
[5] D'Accolti M. *et al*, Scientific Reports, **2023**, *13*(1), 18228.

P054: ELECTROCHEMICAL SENSISG: INNOVATIVE DEVICES AND METHODOLOGIES FOR THE ANALYSES OF DRUGS OF ABUSE

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ABSTRACT

Chemical sensors are compact, inexpensive and easy-to-use measuring devices that quickly provide the desired analytical response and find application in many fields, such as agriculture, security, industry and others.
In this context, my PhD project will focus on the development of electrochemical-type sensors for the identification of the active ingredients present in some of the most common drugs of abuse like cannabinoids, opioids and new psychoactive substances such as synthetic cannabinoids and synthetic opioids. The work will be in collaboration with the Toxicology Laboratory of the Forensic Institute of the Department of Biomedical, Metabolic and Neural Sciences of the University of Modena and Reggio Emilia.
In the last decade, the trafficking and use of illicit drugs showed a continuous incremental trend, remaining worldwide a challenging problem for the consequences on society, health, criminality, and environment. Psychotropic effects promoted by drug consumption indirectly affect the population in terms of increasing number of accidents due to reduced driving ability, drug-related crimes and violence, drug-facilitated sexual assaults, spreading of infectious diseases, etc. [1].
Many of the active ingredients of these abuse drugs are electro-active and therefore research and development of electrochemical sensors capable of detecting them can certainly make an important contribution to all organisations working to control and reduce these problems worldwide.
Once one or more types of matrices, essentially plant-based or synthetic, have been selected for the determination of the active ingredients, the working methodology will be the one represented in **Figure 1**. Different electrodic materials will be investigated as the sensing element to promote selectivity and sensitivity. In this regard, carbon-based electrodes, which have proven to be particularly effective for the analysis of cannabinoids, will be initially tested. Then, MIP (Molecular Imprinted Polymers) deposited on quartz crystal microbalances will be explored to combine electrochemical and gravimetric sensing.
An additional step of the process will be the use of multivariate analysis methods for the interpretation of the articulated analytical signal that could be obtained when working in complex real matrices. This approach will potentially provide information on both the detection and quantification of the active ingredients under analysis.

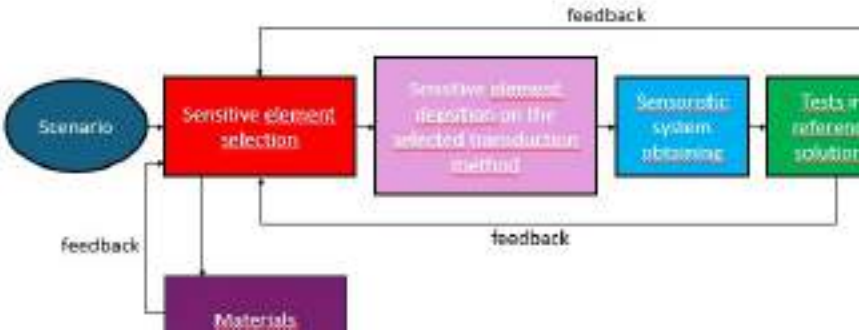

Figure 1. Working methodology for electrochemical sensor development

REFERENCES

[1] B. Zanfrognini, L. Pigani, C. Zanardi, «Recent advances in the direct electrochemilcal detection of drugs of abuse», Journal of Solid State Electrochemistry, 2020, vol. 24, pp. 2603-2616.

P055: ELECTRONIC NOSE COMBINED WITH CHEMOMETRICS TO ASSESS EMERGING MYCOTOXIN CONTAMINATION IN FOOD

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ABSTRACT

Electronic noses (e-noses) based on arrays of gas sensors are emerging as intelligent analytical devices simulating the human nose with high potential for rapid screening and classification of food samples according to their quality, safety and authenticity [1]. E-nose devices are composed of non-selective or semi-selective sensors that interact with volatile aroma compounds to produce electronic signals, which are processed using pattern recognition approaches and classification algorithms such as Principal Component Analysis (PCA), artificial neural networks, and other machine learning classifiers [2].
Mycotoxins, hazardous compounds produced by pathogenic fungi, pose a serious threat to consumer health. For this reason, preventing mycotoxin contamination is crucial for food safety. Regarding contamination of cereals by these naturally occurring toxins, fungal volatile metabolites can be used as an indicator of the presence of mycotoxins in cereals.
In this context, the present study focuses on the development of an analytical approach to rapidly predict contamination from emerging mycotoxins, such as ergot alkaloids, in wheat using an e-nose based on metal oxide semiconductor sensors operating with an enrichment and desorption unit. A central composite design was applied to investigate the effects of extraction temperature and extraction time on the responses of selected volatile compounds; finally, the optimal conditions for the simultaneous extraction of the investigated volatiles were assessed by using the multicriteria method of the desirability functions. For data processing, the responses belonging to the most discriminant sensors were chosen, with the response signal being expressed as the conductance ratio G/G0 as a function of time for each sensor (where G and G0 are the conductance of a sensor in a detection gas and in clean air, respectively). The pattern recognition techniques used for data analysis were PCA, Hierarchical Cluster Analysis and Partial Least Squares-Discriminant Analysis. Results show that the electronic nose can successfully classify durum wheat samples discriminating between non-contaminated and contaminated samples below and above the EU regulatory level [3], demonstrating the potential of this intelligent sensory analysis device for high throughput screening of emerging mycotoxin contamination in wheat.

Acknowledgements: METROFOOD-IT project has received funding from the European Union - NextGenerationEU, PNRR - Mission 4 "Education and Research" Component 2: from research to business, Investment 3.1: Fund for the realisation of an integrated system of research and innovation infrastructures - IR0000033 (D.M. Prot. n.120 del 21/06/2022)

REFERENCES

[1] Rabehi A et al., Appl. Sci., 14 (2024) 4506.
[2] Tan J, Xu J, Artif. Intell. Agric, 4 (2020) 104.
[3] Commission Regulation (EU) 2023/915 on maximum levels for certain contaminants in food and repealing Regulation (EC) No 1881/2006. OJEU L 2023, 119, 66, 103.

P057: FLUORESCENT ANISOTROPY-BASED DISPLACEMENT ASSAY FOR THE IDENTIFICATION OF INHIBITORS TARGETING THE YAP-TEAD INTERACTION INTERFACE

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ABSTRACT

The Hippo signaling pathway regulates cell growth, proliferation, and apoptosis, playing a key role in tumor suppression. Dysregulation of the YAP/TAZ-TEAD interaction drives cancer progression, linking pathway malfunction to poor prognosis and metastasis [1]. Targeting the YAP-TEAD Ω-loop binding site is a promising therapeutic approach. While techniques like ITC, TSA, and SPR have elucidated YAP-TEAD binding, they lack the specificity and throughput needed for efficient inhibitor screening. This study presents a fluorescence anisotropy (FA)-based displacement assay to evaluate inhibitors of the YAP-TEAD protein-protein interaction (PPI). A fluorescently labeled 15-mer peptide (P6TER) [2], modeled on YAP's Ω-loop, interacts with the TEAD4 YBD domain (amino acids 217–434). In solution, P6TER exhibits an anisotropy of 0.14, increasing to 0.27 upon TEAD4 binding, indicating restricted rotational mobility. Introducing inhibitors displaces the labeled peptide, reducing anisotropy toward the baseline, enabling precise binding affinity quantification [3]. The probe binds a well-defined site (interface 3) with a known crystal structure, assuming the ligand binds similarly. The assay was validated with TEAD-targeting compounds, including a library derived from lead compound D361. These compounds showed dissociation constants (Kd) in the low micromolar range, with the most potent at ~600 nM. TEAD inhibitor IAG933 [4], under phase I trials for mesothelioma, demonstrated consistent Kd values (~10 nM), confirming assay reliability. This FA-based platform offers a high-throughput method to discover inhibitors disrupting YAP/TEAD oncogenic pathways.

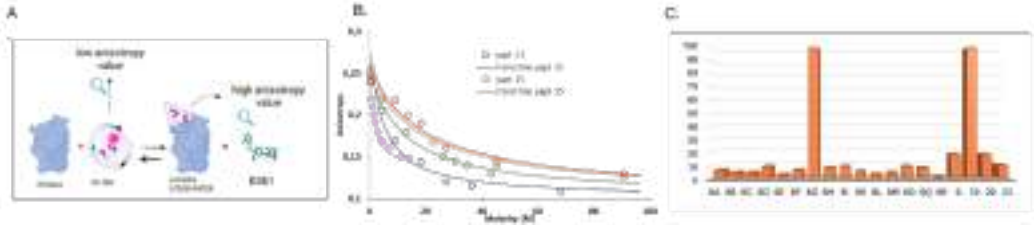

Figure 1: A. graphical scheme of anisotropy assay B. Fitting of the results through the mathematical expression of Wang C. Kd calculated for each compound tested (μM)

[1] J. C. Hau *et al.*, "The TEAD4-YAP/TAZ Protein-Protein Interaction: Expected Similarities and Unexpected Differences," *ChemBioChem*, vol. 14, no. 10, pp. 1218–1225, 2013, doi: 10.1002/cbic.201300163.
[2] P. Furet *et al.*, "Structure-based design of potent linear peptide inhibitors of the YAP-TEAD protein-protein interaction derived from the YAP omega-loop sequence," *Bioorganic Med. Chem. Lett.*, vol. 29, no. 16, pp. 2316–2319, 2019,
[3] Z. X. Wang, "An exact mathematical expression for describing competitive binding of two different ligands to a protein molecule," *FEBS Lett.*, vol. 360, no. 2, pp. 111–114, 1995, doi: 10.1016/0014-5793(95)00062-E.
[4] Chapeau, E. et al, (2024). Direct and selective pharmacological disruption of the YAP–TEAD interface by IAG933 inhibits Hippo-dependent and RAS–MAPK- altered cancers. *Nature Cancer*, *5*(7), 1102–1120. https://doi.org/10.1038/s43018-024-00754-9

P058: DEVELOPMENT AND APPLICATION OF AN HPLC-UV-VIS METHOD FOR PHENOLIC COMPOUND QUANTIFICATION IN AQUEOUS MATRIX

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ABSTRACT

Phenolic compounds are among the major contaminants of water sources, as they are released into water bodies through both natural and anthropogenic activities. Anthropogenic sources of phenols in water bodies include industrial, agricultural, domestic, and municipal activities[1]. Phenols pose significant health risks, including genetic aberrations, endocrine dysregulation, and destruction of the immune system; consequently, their persistence in water bodies endangers humans, animals, and aquatic life[2]. State-of-the-art techniques for the removal of phenols from water bodies consist of adsorption, biological treatment, advanced oxidation processes, and filtration[1]. Despite the various techniques available, the exceeding of limit values set by environmental protection agencies leads to the need to develop new strategies for the identification and removal of phenolic compounds from water bodies to protect environmental and public health.
In this light, we develop an analytical procedure to evaluate the ability of novel nano-structured materials to adsorb phenols in an aqueous medium. In detail, we developed a reverse phase chromatographic method (RP-HPLC) coupled with a UV-Vis detection to quantify phenols in water matrix. Six phenols reported in the Priority Pollutant List of the United States Environmental Protection Agency (EPA, 2014)[3], namely phenol, 4-nitrophenol, 2-chlorophenol, 2-nitrophenol, 4-chloro-3-methylphenol, and 2,4-dichlorophenol, were selected for the study. The HPLC-UV-Vis method was validated according to the International Council on Harmonization (ICH) guidelines, and applied to evaluate the adsorbent ability of nano-structured materials, based on bentonite, titanium dioxide, sepiolite, silica, and phaeodactylum tricornutum.
Adsorption yield was determined by incubating a phenols mixture with each nano-structured material at room temperature and under continuous stirring for 24h; at selected time points the adsorbent was removed by centrifugation, and the supernatant was subjected to analysis. These studies allowed the i) identification of the most promising materials, ii) evaluation of particle size impact on materials adsorption capacity, and iii) the evaluation of the light-induced activation of those materials containing titanium dioxide. Moreover, to better characterize the most promising nano-structured materials, kinetic studies were extended to 72 h.

REFERENCES

[1] Said, K.A.M., Ismail, A.F., Karim, Z.A., Abdullah, M.S., Hafeez, A., Process Safety and Environmental Protection, 2021, 151, 257–289.
[2] Plessis, M. du, Fourie, C., Stone, W., Engelbrecht, A., *Biochimie*, 2023, 209, 103–115.
[3] EPA, 2014. Priority pollutant list. Environmental Protection Agency of United States. Available in: https://www.epa.gov/sites/production/files/2015-09/documents/priority-pollutant-list-epa.pdf. (Accessed November 2024)

P059: STUDY OF THE OXIDATION REACTION OF CYCLOHEXANE AND TETRAHYDROFURAN BY PHOTOELECTROCHEMICAL METHODS USING TUNGSTEN OXIDE ELECTRODES

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ABSTRACT

In the field of fine chemistry, there is an increasing demand towards the development of new, sustainable reactions that enable the synthesis of molecules of industrial and pharmaceutical interest with specific reactivity and functionalities. Within this framework, the introduction of oxygen atoms in cyclic organic compounds can be employed to obtain important platform chemicals. By the following assumptions, this work aims to develop a heterogeneous system that promotes the oxidation of organic substrates under environmentally friendly conditions with the use of light as a reactant. In particular, the work targets the photoelectrochemical oxidation of cyclohexane (CHA) and tetrahydrofuran (THF) using WO_3 electrodes to attain KA-OIL mixture and gamma-butyrolactone, respectively. In this regard, two different WO_3 electrodes were tested, solvothermal and colloidal electrodes. Furthermore, in the following communication we will show how the different photoelectrochemical behavior of the two typologies of electrodes can influence the trend of the reaction in terms of faradic efficiency (F.E.) and we will report our mechanistic proposal for the photoelectrochemical oxidation of CHA and THF.

P060: PRELIMINARY EVALUATION OF NANOFIBERS CAPABILITY IN SOUND ABSORPTION

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ABSTRACT

Noise reduction is one of the main tasks to be addressed in the field of automotive and aerospace industries. The study and improvement of acoustic properties is of paramount importance when seeking an increase in comfort. To address both noise absorption and sustainability, the use of nanofibers can be a valid option in order to guarantee as well material reduction using lightweight nonwoven mats. Indeed, nanofibers possess many attractive features that make them excellent candidates for many applications, including in tissue engineering, drug delivery systems, wound dressings, scaffolds for regenerative medicine and as well as toughenersfor increased mechanical performance. Their ability to be easily produce via electrospinning process, together with their light weight, reduced dimensions and high possibility to tune their properties makes them extremely interesting as well in possibly enhance or at least modify the acoustic properties of conventional materials, both alone and coupled with them. Indeed, just by changing characteristics like fibre diameter, membrane grammage, fibre orientation, and constituent polymer, customized and tailorable chemical, mechanical, and physical properties can be obtained[1]. However, the mechanism and the relationship between nanofibrous membranes and enhanced noise absorption is yet far from being understood and established.
Nowadays, different approaches are under investigation, that involve considering them as bulk materials, even if their structure is extremely porous, considering them as membrane resonators and coupling them with another conventional material [2]–[4]. Consequently, one limitation stands in the fact that the measurement setup for the characterization of the acoustic properties of the nanofibrous mats is therefore far from being clear and standardized. This leads to the need of understanding whether the testing methods that are currently used for the evaluation of the acoustic performance of macro-dimensioned material can be efficiently applied as well on nanostructured materials.
In the present work, two nanofibrous diameter and two grammages have been produced and tested, prior adequate process optimization, to evaluate the effect of these parameters on the acoustic absorption properties. The acoustic properties of samples were analyzed using an impedance tube and one-microphone technique, allowing analysis in the 400-4000 Hz frequency [2].
The preliminary tests show some capability of the nanofibrous mats on the sound absorption, paving the way for their use in practical applications.

REFERENCES

[1] A. Hurrell, K. V. Horoshenkov, S. G. King, and V. Stolojon, "On the relationship of the observed acoustical and related non-acoustical behaviours of nanofibers membranes using Biot- and Darcy-type models," *Appl. Acoust.*, vol. 179, p. 108075, Aug. 2021, doi: 10.1016/j.apacoust.2021.108075.
[2] K. Kalinová, "Nanofibrous Resonant Membrane for Acoustic Applications," *J. Nanomater.*, vol. 2011, pp. 1–6, 2011, doi: 10.1155/2011/265720.
[3] V. Chen, I. Perez Pablos, and J.-M. Chen, "Acoustic characterization of nanofibers for optimization with porous substrate," *J. Acoust. Soc. Am.*, vol. 153, no. 1, pp. 40–49, Jan. 2023, doi: 10.1121/10.0016811.
[4] S. Akasaka, T. Kato, K. Azuma, Y. Konosu, H. Matsumoto, and S. Asai, "Structure-sound absorption property relationships of electrospun thin silica fiber sheets: Quantitative analysis based on acoustic models," *Appl. Acoust.*, vol. 152, pp. 13–20, Sep. 2019, doi: 10.1016/j.apacoust.2019.03.016.

P061: EFFECT OF RAW MATERIALS, MOISTURE AND BINDER ON THE GRANULATION PROCESS OF FERTILIZER AND SOIL IMPROVERS

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ABSTRACT

The objective of this study was to investigate the influence of the chemical and physical nature of the raw materials (synthetic and or natural), of the possible additives added, of different process variables and binders, and chemical-physical parameters on the quality and efficiency of wet granulation in terms of: i)- yield of the granulation process in the dimensional range of 0,5-1,4 / 2–4 mm; ii) sustainability of the granulation process (reduction in water and energy consumption and CO2 emission); iii) chemical-mechanical properties of the granules (solubility, durability, …) and iv) minimization of the production cost. Since the value of the fertilizer is given by: i) maximum titration and absence of inert materials; ii) maximum solubility in water; iii) homogeneous grain size with absence of dust; iv) purity and characteristics of the raw materials, to allow the simultaneous solubilization/ bioavailability of all the nutritional elements.
The analysis of the results shows the following conclusions regarding the variables that most influence the granulation process and the chemical-mechanical properties of the granules: i) raw materials with higher solubility help granulation process and dissolution in water/soil of the granules; ii) additives influences quantity and type of binder solution, yield of production and chemical-mechanical properties; iii) finer powder requires a larger amount of water/binder solution to granulate due to higher surface area. Coarser powder gives granules less soluble in water /soil but more durable increasing percentage of binder also yield of production increase (in this case the limit could be due to the production cost and higher technological characteristics not needed). The type and quantity of the binder influence break load, durability, porosity, temporal stability and quick dissolution in water/soil of the granules; it does not appear to influence the compactness. The binder with higher solubility in water help granulation process and quick dissolution in water/soils of the granules. Moreover, an inverse relationship between porosity and grain hardness seems to be present.

P062: EXTRACTION, CANNABINOID PROFILING AND EVALUATION OF THE ANTIPROLIFERATIVE ACTIVITY AGAINST GLIOBLASTOMA MULTIFORME CANCER CELLS OF NON-PSYCHOACTIVE *CANNABIS SATIVA* L.

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ABSTRACT

Glioblastoma multiforme (GBM) is one of the most frequent malignant and lethal form of brain cancer. The conventional therapy for GBM includes surgery, radiation therapy and chemotherapy with temozolomide (TMZ), a DNA alkylating agent. GBM is characterized by high proliferation rate, invasion, migration, angiogenesis and resistance to conventional anticancer drugs. Many studies have shown the potential antiproliferative activity of cannabinoids on different type of cancer [1]. Cannabinoids are the typical terpenophenolic compounds from *Cannabis sativa* L. This plant has a very complex chemical profile, and the most abundant compounds in the fresh plant material are cannabinoic acids, that undergoes to a spontaneous non-enzymatic decarboxylation generating their corresponding neutral counterparts. Among non-psychoactive cannabinoids, cannabidiol (CBD) has shown to possess several biological activities, including antioxidant, anti-inflammatory, neuroprotective and antiseizure activity [2]. CBD has also demonstrated to possess the capacity to decrease cancer cell proliferation [3]. Since CBD is able to cross the blood brain barrier (BBB), it is supposed to explicate antiproliferative activity against CNS cancers, such as GBM. In the light of this, the aim of this study was to evaluate the antiproliferative activity of a cannabinoid enriched fraction (CEF), extracted and fully characterized from inflorescences of non-psychotropic *C. sativa*, and to assess the bioactivity *in vitro* against GBM cancer cell lines (U87 and T98G). The analysis of CEF was carried out by targeted metabolomics using UHPLC-HRMS [4], with CBD being the main compound as confirmed by quantitative analysis using HPLC-UV [5]. Cell viability was assessed after 24 and 48 h of exposure with CEF and CBD on U87 and T98G human GBM cancer cell lines, using TMZ as the positive control. It was observed that CEF and CBD treatments gave comparable results in terms of inhibition of cell viability in a time and dose-dependent manner for both cell lines. The mechanism/s responsible for the activity of CEF and CBD against GBM are currently under investigation.

REFERENCES

[1] Faiz M. B., Naeem F., Irfan M., Aslam M. A., Estevinho L. M., Ateşşahin D. A., Alshahrani A. M., Calina D., Khushbukhat K., Sharifi-Rad J. Exploring the therapeutic potential of cannabinoids in cancer by modulating signaling pathways and addressing clinical challenges *Discover Oncology* **(2024)** *15*(1), 490. [2] Lee S., Lee Y., Kim Y., Kim H., Rhyu H., Yoon K., Lee C.-D., Lee S. Beneficial effects of cannabidiol from Cannabis *Applied Biological Chemistry* **(2024)** *67*(1), 32. https://doi.org/10.1186/s13765-024-00867-w;
[3] Anceschi L., Codeluppi A., Brighenti V., Tassinari R., Taglioli V., Marchetti L., Roncati L., Alessandrini A., Corsi L., Pellati, F. Chemical characterization of non-psychoactive *Cannabis sativa* L. extracts, in vitro antiproliferative activity and induction of apoptosis in chronic myelogenous leukaemia cancer cells *Phytotherapy Research* **(2022)** *36*(2), 914–927. https://doi.org/10.1002/ptr.7357;
[4] Berman P., Futoran K., Lewitus G. M., Mukha D., Benami M., Shlomi T., Meiri D. A new ESI-LC/MS approach for comprehensive metabolic profiling of phytocannabinoids in Cannabis *Scientific Reports* **(2018)** *8*(1), 14280. https://doi.org/10.1038/s41598-018-32651-4;
[5] Durante C., Anceschi L., Brighenti V., Caroli C., Afezolli C., Marchetti A., Cocchi M., Salamone S., Pollastro F., Pellati F. Application of experimental design in HPLC method optimisation for the simultaneous determination of multiple bioactive cannabinoids. *Journal of Pharmaceutical and Biomedical Analysis* **(2022)** *221*, 115037.

P063: TARGETED ANTIBIOTIC DELIVERY USING HYDROXYAPATITE-AMPICILLIN COMPOSITES

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ABSTRACT

Introduction
Calcium orthophosphates, particularly hydroxyapatite (HA), are vital for both natural and synthetic applications, such as bone and tooth composition. HA's stability and low solubility make it suitable for biomaterials and biomedical uses like drug delivery [1][2]. This study focuses on embedding ampicillin into HA matrices for enhanced antibiotic delivery in medical applications [3].

Experimental methods
Hydroxyapatite synthesis involved high-temperature reactions using calcium nitrate and ammonium phosphate. Antibiotic-enriched hydroxyapatites were created by adding ampicillin to the phosphate solution. Characterization includes X-ray diffraction (XRD), Fourier transform infrared spectroscopy (ATR-FTIR), thermogravimetric analysis, electron microscopy for morphological studies and microbiological test.

Results and discussion
X-ray diffraction patterns confirmed that ampicillin addition during HA synthesis did not affect the crystalline structure of HA, maintaining its integrity—essential for biomedical applications. ATR-FTIR results corroborated this, showing characteristic HA absorption bands, indicating that the chemical structure remained unchanged with ampicillin integration. Electron microscopy affirmed HA's morphology and thermogravimetric analysis revealed a weight loss in the ampicillin-infused HA, indicating the antibiotic's presence and
its interaction within the HA matrix.

Conclusion
This study confirms that ampicillin integration into the HA matrix maintains its crystalline purity. Using XRD and ATR-FTIR, the study verified HA's structure and amp incorporation. Thermogravimetric analysis quantified the ampicillin, indicating its potential.
for controlled delivery. These results suggest significant benefits for infection control in orthopedic and dental implants.

REFERENCES

[1] A. Bigi and E. Boanini, 'Fuctionalized biomimetic calcium phospates for bone tissue repair', *J Appl Biomater Funct Mater*, vol. 15, pp. 313-325, May 2017, doi: 10.5301/jabfm.5000367.
[2] E. Boanini *et al.*, 'Ionic substitutions in calcium phosphates synthesized at low temperature', *Acta Biomaterialia*, vol. 6, pp. 1882–1894, December 2009, doi: 10.1016/j.actbio.2009.12.041.
[3] A.C. Queiroz *et al.*, 'Adsorption and release studies of sodium ampicillin from hydroxyapatite and glass-reinforced hydroxyapatite composites', *Biomaterials*, vol. 22, pp. 1393–1400, June 2001, doi: 10.1016/s0142-9612(00)00296-9.

P064: LIPOSOMAL FORMULATION FROM AGRO-INDUSTRIAL WASTES: ECO-FRIENDLY SOLUTIONS FOR COSMECEUTICALS AND NUTRACEUTICALS

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ABSTRACT

The valorization of agro-industrial wastes for the sustainable production of bioactive and nutraceutical compounds represents an innovative approach in medicinal chemistry.[1] Technical cashew nutshell liquid (tCNSL), an inexpensive and abundant by-product from *Anacardium occidentale* nut processing, is a natural source of phenolic lipids, including cardanols, cardols, 2-methylcardols, and traces of anacardic acids, characterized by a long pentadecyl side chain with varying degrees of unsaturation. These bioactive compounds exhibit biological activities, such as antioxidant and anti-inflammatory properties,[2] making CNSL an attractive candidate for cosmeceutical and nutraceutical applications. In this study, CNSL was incapsulated into liposomal formulations to enhance the bioavailability, stability, and safety profile of its bioactive constituents,[3] thoroughly evaluating particle size, encapsulation efficiency, stability, and controlled release profiles. *In vitro* studies on human keratinocytes (HaCaT) and monocytes (THP-1) under oxidative stress conditions revealed the biocompatibility and protective effects of CNSL liposomes, with significant reductions in cell death, as assessed by flow cytometry, and inflammation markers, measured by qPCR. Moreover, scratch assays demonstrated CNSL liposomes' ability to improve cell migration, therefore suggesting improved wound healing properties, and highlighting their potential for cosmetic and anti-aging applications. Complementary *in vivo* assays in *Caenorhabditis elegans* models confirmed the absence of toxicity. In conclusion, biowaste-derived CNSL liposomal systems represents a promising and sustainable approach for developing new bioactive products. This work leverages natural, readily available biowaste for innovative health applications while supporting a circular economy and advancing green medicinal chemistry.

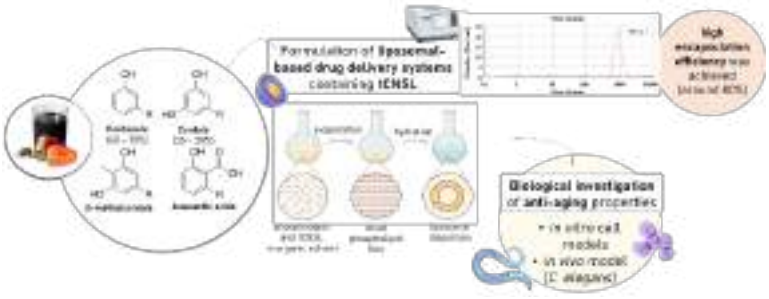

Figure 1. Formulation of CNSL-based liposomes and *in vitro*/*in vivo* biological investigation.

REFERENCES

[1] Espro, C.; Paone, E.; Mauriello, F.; Gotti, R.; Uliassi, E.; Bolognesi, M. L.; Rodríguez-Padrón, D.; Luque, R. Sustainable Production of Pharmaceutical, Nutraceutical and Bioactive Compounds from Biomass and Waste. *Chem. Soc. Rev.* **2021**, *50* (20), 11191–11207. https://doi.org/10.1039/d1cs00524c.

[2] Hemshekhar, M.; Sebastin Santhosh, M.; Kemparaju, K.; Girish, K. S. Emerging Roles of Anacardic Acid and Its Derivatives: A Pharmacological Overview. *Basic Clin. Pharmacol. Toxicol.* **2012**, *110* (2), 122–132. https://doi.org/10.1111/j.1742-7843.2011.00833.x.

[3] Akbarzadeh, A.; Rezaei-sadabady, R.; Davaran, S.; Joo, S. W.; Zarghami, N. Liposome : Classification , PrepNew Aspects of Liposomesaration , and Applications. *Nanoscale Res. Lett.* **2013**, *8* (102), 1–9.

P066: MICROFLUIDIC OPTIMIZATION OF CHOLESTEROL NANOPARTICLES: ADVANCING TOWARDS INDUSTRIAL APPLICATIONS AND GENE THERAPY

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ABSTRACT

Despite the recent approvals of multiple nanoparticle (NP) therapies, upscaling their production to meet industrial requirements is still a major obstacle to overcome. In this perspective, in this study we used a method suitable for industrial-scale production, i.e. the microfluidic mixing technique, to formulate engineered NPs to treat Huntington's Disease (HD). HD is a genetic disease linked to a defective production of a protein called huntingtin (HTT), but recent studies revealed that a decreased cholesterol (CHOL) level in the brain is also involved, concurring to neuronal degeneration[1,2]. Direct CHOL delivery to the brain using CHOL-loaded NPs already displayed beneficial effects restoring cognitive and motor impairments in HD models[3], but the formulation suffers from scalability issues. Based on these results, we optimized a microfluidic method to produce CHOL NPs loaded with siRNA to achieve a dual therapeutic approach: siRNA will lower the production of mutant HTT, while the composition of the NPs itself will help restore physiological concentrations of CHOL in damaged neurons. An initial screening study was conducted using a syringe pump to investigate how the operative parameters impacted the formation of NPs, and to identify optimal compositions in terms of the flow rate ratio, CHOL concentration, and surfactant amount, aiming to maximize CHOL's concentration in the final product to deliver the highest possible dosage to the brain, using minimum surfactant. To encapsulate genetic material, additional studies were done to implement a synthetic, cationic derivative of CHOL (DC-CHOL) in the formulation. Encapsulation experiments were carried out with a negative control siRNA to determine if the method was suitable for this purpose. Once the most promising candidates had been identified, the method was translated to an Automated NanoParticle system suitable for industrial-scale production, and an additional screening study was performed to further optimize the method for a fully scalable production. All NPs produced were characterized in terms of size (< 300 nm), polydispersity index (PdI < 0.3), zeta potential, and storage stability at 4°C and -20°C (with and without cryoprotectants). Weight yield and morphological analysis were also performed on the most promising candidates, and encapsulation efficiency was determined for siRNA-loaded NPs assembled with the two instruments. This study demonstrates the potential of the microfluidic mixing technique for the industrial production of NPs as delivery systems for gene therapy. Further studies will concern *in vitro* and *in vivo* studies with a specific therapeutic siRNA, hopefully bridging the lab-to-industrial gap to achieve the mass-scale production of an efficient nanoformulation against HD.

REFERENCES

[1] Leoni et al.. *Biochimica et Biophysica Acta (BBA) - Molecular and Cell Biology of Lipids*. **2015**;1851(8):1095-1105. doi:10.1016/j.bbalip.2014.12.018

[2] Valenza M, Carroll JB et al.. *Human Molecular Genetics*. **2007**;16(18):2187-2198. doi:10.1093/hmg/ddm170

[3] Valenza M, Chen JY et al. *EMBO Molecular Medicine*. **2015**;7(12):1547-1564. doi:10.15252/emmm.201505413

P067: SYNTHESIS OF MUGINEIC ACID FAMILY PHYTOSIDEROPHORE ANALOGUES AS LOW-COST AND SUSTAINABLE IRON FERTILIZERS FOR AGRICULTURE IN POOR SOIL

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ABSTRACT

Plants, like all living organisms, require a wide range of essential nutrients to support fundamental physiological processes that are vital for their growth, development, and defense against environmental stress. When these nutrients are deficient or unavailable in the soil, plants become vulnerable to a variety of adverse effects that can undermine their health and productivity. One common and damaging nutrient deficiency is iron chlorosis, which frequently occurs in plants grown in calcareous soils. This condition manifests as yellowing of the leaves, a significant reduction in crop yield, and, in severe cases, the death of individual plant parts or the entire plant.
The primary solution for combating iron chlorosis is the application of iron chelates as fertilizers. However, the production methods for most commercial chelating agents -developed in the 1970s- are unsustainable, contribute to pollution, and are costly. As such, there is an urgent need to explore more innovative and sustainable methods for producing these fertilizers, ensuring both cost-effectiveness and environmental responsibility.
One promising approach comes from the work of Professor Namba's research group, which demonstrated that soil application of synthetic 2′-deoxymugineic acid (DMA)—a natural phytosiderophore derived from the Poaceae family—can alleviate iron deficiency in plants grown in calcareous soils.[1] Unfortunately, the high cost and poor stability of synthetic DMA hinder its practical agricultural use. In this study, we present a solution by developing proline-derived analogues of DMA (PDMA) that are both more stable and cost-effective. Through practical synthesis, density functional theory (DFT) calculations, and biological testing, we demonstrate that these PDMA analogues can form stable complexes with Fe(III) and offer a viable alternative to synthetic DMA for addressing iron deficiency in plants.

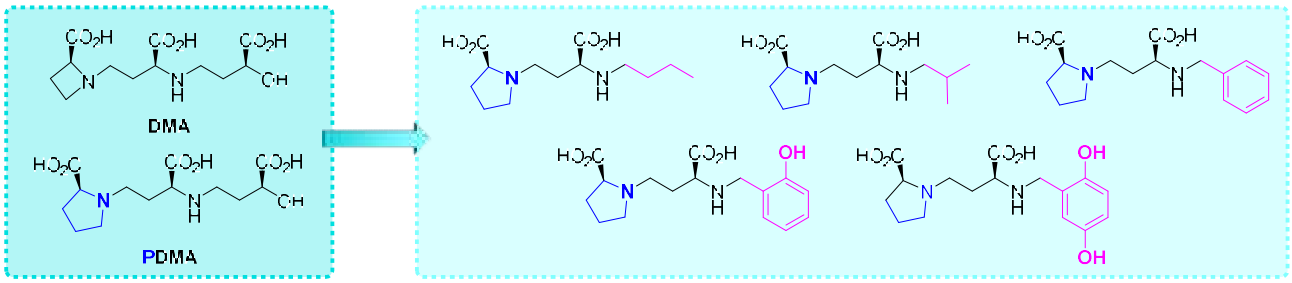

Figure 1: Previous results (left) and new differently substituted synthetic analogues of PDMA (right).

This publication is part of the project PNRR-NGEU which has received funding from the MUR – DM352/2022

REFERENCES

[1] M. Suzuki, A. Urabe, S. Sasaki et al., Nature Communications 2021, 12, 1558.

P068: SYNTHESIS AND CHARACTERIZATION OF BIO-BASED UNSATURATED POLYESTER RESINS FOR SUSTAINABLE POLYMER APPLICATIONS

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ABSTRACT

In recent years, rising environmental awareness has led to a strong interest in replacing non-renewable, petroleum-based materials with renewable alternatives. While a gradual shift toward bio-based production is occurring across various sectors, the production of widely used chemical products – particularly polymers – shows exceptional promise. Among these, unsaturated polyester resins (UPRs) are especially valued for their excellent mechanical processability, resistance to heat and chemicals, and high electrical conductivity. These properties make UPRs essential materials in industries such as transportation, construction, coatings, electronics, and more [1]. However, most commercially available UPRs are synthesized from petrochemical sources, consisting of two main components: unsaturated polyester and reactive diluents. The project aims to identify or synthesize new bio-based raw materials for UPR production from renewable sources. Two partially bio-based unsaturated polyester resins were successfully synthesized through polycondensation, using both renewable and non-renewable raw materials. The unsaturated polyester pre-polymers, as well as the cross-linked polyester resins, were characterized to assess their potential applications. Characterization includes evaluation of the chemical properties (via IR, ^{1}H-NMR, ^{13}C-NMR, GPC), mechanical and thermos-mechanical properties (TMA, DMA, Stress/Strain behaviour), and thermal stability (DSC, TGA) of the resins. The resulting data were compared with that of a common "general-purpose" unsaturated polyester resin made from petroleum-derived raw materials. This project seeks to demonstrate the feasibility of bio-based materials in polyester resin production, supporting a transition toward more sustainable polymer solutions. The project is conducted in collaboration with Carlo Riccò & F.lli S.p.A., a local company specializing in the industrial production of unsaturated polyester resins.

REFERENCES

[1] Q. Li, S. Ma, X. Xu, e J. Zhu, "Bio-based Unsaturated Polyesters", in *Unsaturated Polyester Resins*, Elsevier, 2019, pp. 515-555. doi: 10.1016/B978-0-12-816129-6.00020-X.

P069: EXPLORING THE INTERACTION BETWEEN HUMAN NEUROGLOBIN AND SULPHIDE

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ABSTRACT

In this study, electronic absorption spectroscopy was used to analyse the in vitro reactivity of WT human neuroglobin (hNgb) and its C46AC55A mutant with sulphide species, to better understand hNgb physiological role.

In the last two decades, the knowledge of sulphide's biology in organisms expanded, from just a toxic gas (as H_2S) to an endogenously produced signalling molecule involved in many diseases (like schizophrenia, Alzheimer's, cardiovascular and metabolic disorders). The ability of sulphide species to interact with ferric heme-proteins and the identity of the Fe-bound species (H_2S, HS^- or S^{2-}) are not fully understood [1].

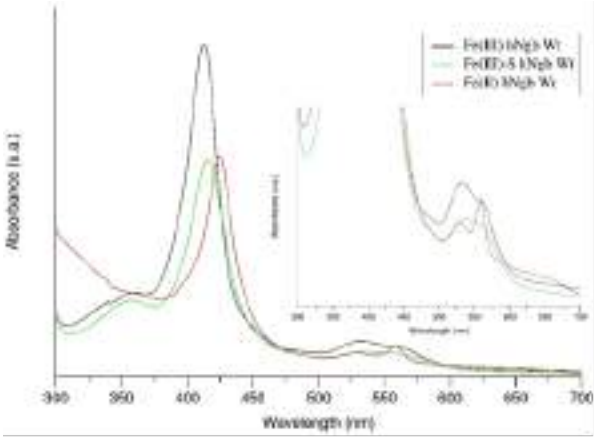

Figure 1: UV-Vis spectra of WT Fe(II)-Ngb upon addition of sulphide excess ratio (600 fold) at pH 7.0 in anaerobic conditions, in the inset detail of Q bands

Neuroglobin is a small monomeric globin, located primarily in retinal and neuronal cells, containing a single heme *b* group, whose axial coordination positions are occupied by two histidines. Therefore, the binding of exogenous species requires the cleavage of the bond between the iron and the distal histidine (H64) [2]. Over-expression of Ngb in mice highlighted a role in cell survival in hypoxic/ischemic or oxidative stress conditions and in neurodegenerative diseases. Many physiological functions have been hypothesized: oxygen transport, apoptosis inhibition, nitrite reduction and sulphide signalling [1,3]. Under oxidizing conditions, Cys46 and Cys55 residues of WT hNgb form an internal disulfide bridge, which is cleaved in a reducing environment, as observed in the cytoplasm. Therefore, the C46AC55A mutant mimics hNgb in physiological conditions. Cleavage of the S-S bond induces a conformational rearrangement, reducing the accessibility of the heme pocket and strengthening the iron-histidine bond [4].

Under anaerobic conditions at physiological pH in presence of an excess of Na_2S (protein:sulphide molar ratio = 1:600), a two-step reaction occurs:

1. Formation of a six-coordinated Fe(III)-S adduct, with a shift of the Soret and Q-bands.
2. Internal electron transfer within the Fe(III)-S adduct, producing a low-spin six-coordinated Fe(II), followed by the formation of sulfoheme(II), probably resulting from the reaction of a $HS^{\cdot}$ radical with the tetrapyrrolic ring [5].

Kinetics of reaction were analysed at different pH values, between 6.0 and 13.0. The reaction rates of WT and C46AC55A with sulphide decrease from pH 6.0 to 10.0 and increase up to pH 13.0. Moreover, above pH 10.0 formation of sulfoheme(II) isn't observed, suggesting changes in the reaction mechanism possibly connected to the sulphide speciation. It appears that the interaction between hNgb and sulphide species involves H_2S or S^{2-} rather than HS^-. The higher reaction rate of the C46AC55A mutant compared to WT suggests that the reduced solvent accessibility and stronger axial coordination of the iron are not limiting factors for sulphide binding.

REFERENCES

[1] A. Domán et al., *Redox Biology*, **2023**, *60*, 102617.
[2] T. Hankeln et al., *Journal of Inorganic Biochemistry*, **2005**, *99*, 110-119.
[3] P. Ascenzi et al., *Molecular Aspects of Medicine*, **2016**, *52*,1-48.
[4] D. Hamdane et al., *Journal of Biological Chemistry*, **2003**, *278 (51)*, 51713-51721.
[5] J. A. Berzofsky et al., *Journal of Biological Chemistry*, **1971**, *246 (10)*, 3367-3377.

P070: DESIGN OF AN ENGINEERED PHAGE NANOVECTOR FOR EGFR-TARGETED PHOTODYNAMIC THERAPY

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ABSTRACT

Photodynamic therapy (PDT) is a clinically approved therapeutic modality for cancer. PDT is characterized by high selectivity and minimal side effects [1]. The success of PDT is usually limited by the lack of selective accumulation of the photosensitizer (PS) in cancer cells, resulting in unwanted phototoxicity [2].
Temoporfin (mTHPC), a clinically approved chlorin-based PS, has a very high potential in PDT. However, its application is hampered by its lipophilic character. Human Serum Albumin (HSA), the most abundant carrier protein in the blood, can be used as supramolecular host for mTHPC (mTHPC@HSA) [3].
Bacteriophages (phages) are ubiquitous viruses that infect bacteria but are inactive against eukaryotic cells. Refactored M13 phages, with targeted tropism against EGFR [4,5], were generated through phage display of a nanobody able to recognize the EGF receptor. Using SPAAC (strain promoted azide alkyne cycloaddition) click chemistry reaction, the surface of the viral capsid was decorated with the supramolecular complex mTHPC@HSA. With this orthogonal workflow, M13 was transformed into a selective carrier for mTHPC, improving both its selectivity and biocompatibility.
The PDT killing activity of cancer cells was observed at picomolar concentrations of the refactored phage.

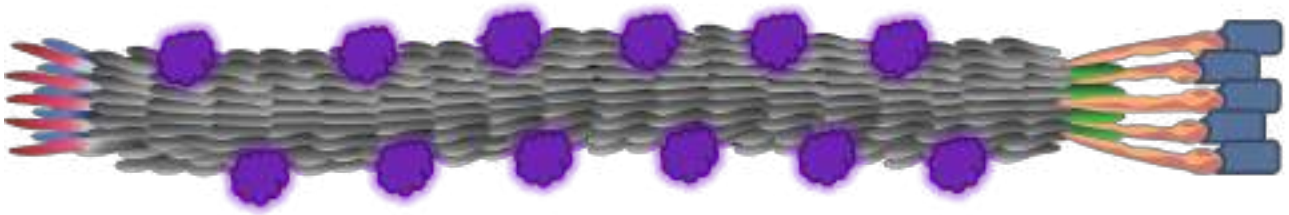

Figure 1. Graphical representation of mTHPC@HSA-M13$_{7D12}$ nanovector

REFERENCES

[1] D. E. J. G. J. Dolmans , D. Fukumura and R. K. Jain , Nat. Rev. Cancer, 2003, 3 , 380 —387
[2] Ulfo, L.; Costantini, P.E.; Di Giosia, M.; Danielli, A.; Calvaresi, M. EGFR-Targeted Photodynamic Therapy. Pharmaceutics 2022, 14, 241.
[3] Mattioli, E.J.; Ulfo, L.; Marconi, A.; Pellicioni, V.; Costantini, P.E.; Marforio, T.D.; Di Giosia, M.; Danielli, A.; Fimognari, C.; Turrini, E.; et al. Carrying Temoporfin with Human Serum Albumin: A New Perspective for Photodynamic Application in Head and Neck Cancer. Biomolecules 2023, 13, 68.
[4] Ulfo L, Cantelli A, Petrosino A, Costantini PE, Nigro M, Starinieri F, Turrini E, Zadran SK, Zuccheri G, Saporetti R, Di Giosia M, Danielli A, Calvaresi M. Orthogonal nanoarchitectonics of M13 phage for receptor targeted anticancer photodynamic therapy. Nanoscale. 14, 632-641
[5] P. E. Costantini, R. Saporetti, M. Iencharelli, S. Flammini, M. Montrone, G. Sanità, V. De Felice, E. J. Mattioli, M. Zangoli, L. Ulfo, M. Nigro, T. Rossi, M. Di Giosia, E. Esposito, F. Di Maria, A. Tino, C. Tortiglione, A. Danielli, M. Calvaresi, Phage-Templated Synthesis of Targeted Photoactive 1D-Thiophene Nanoparticles. Small 2024, 2405832.

P071: ENCAPSULATION OF ORGANIC UV FILTERS IN ZEOLITE MATRIX AND THEIR INCLUSION IN FOTOPROTECTOR STICK

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ABSTRACT

The number of annually diagnosed skin cancers, including both malignant melanoma and non-melanoma skin cancer, is growing year after year. A primary prevention strategy is the use of sunscreens. Several formulations containing chemical (organic) and physical (inorganic) UV filters have been developed. Organic UV filters (UVfs) are the most popular and widely used in sunscreens. Different chemical filters are mixed to achieve broad protection from UVA to UVB radiations. However, several open issues are still related to the sunscreen products, in fact, it is known that most of the used filters are photolabile. If the absorbed energy in not dissipated, the molecule degrades and it transforms in another entity of unknown toxicity and no longer efficient in protecting from UV rays. The use of inorganic scaffolds - such as hydrotalcites, amorphous silica, mesoporous materials and zeolites- has been proposed to increase sunscreen stability and prevent absorption through the skin. In most of the cases, the encapsulation systems were found to be generally effective, but a rapid release of the UVfs was observed.
The UV filters currently used in cosmetic formulations are octyl methoxycinnamate (*octinoxate*, OMC;) and 4-tert-butyl-4-methoxydibenzoylmethane (*avobenzone,* AVO). These UVfs were chosen as a model in this project because they degrade under exposure to UV radiation and also due to their reactions with other constituents of the formulations. It has been demonstrated that the presence of both these filters in a formulation can lead to destructive interactions with consequent loss of effectiveness. These UVfs will be separately incorporated into the synthesised zeolite frameworks (LTL type) to increase their stability [1-3].
Zeolite-UV filter hybrids (ZeoAVO and ZeoOMC) will avoid the abovementioned issues by encapsulating molecular UV filters in an inert, bio-compatible porous matrix. This innovation will prevent direct contact of the filters with skin and other formulation components making them safer and more photostable. A detailed chemical-physical characterization was conducted to understand the effects of spatial confinement on the photobehaviour of the filters.
To improve its applicability in the cosmetic field, the grain size of the zeolite has been reduced. We also tried to coat the zeofilter particles with two types of coatings (magnesium stearate and chitosan) to prevent the release of the filters from the pores of the zeolite, once the filter was in formulation. The release of coated and uncoated zeofilters for in artificial sweat was compared to simulate their use in real conditions, obtaining promising results.
Finally, a photoprotector cosmetic stick were formulated containing the zeofilters, obtaining a stick that was easy to compose and produce, non-greasy on the skin, pleasant to the touch and with a good flowability.

REFERENCES

[1] R. Arletti et al. European Patent Office, patent WO/2022/185348.
[2] G. Confalonieri et al., Microporous and Mesoporous Materials, 344 (2022) 112212.
[3] R. Fantini et. al, Journal of Photochemistry and Photobiology A: Chemistry,452 (2024)115585.

P072: THE ROLE OF WATER ON CARBON DIOXIDE AND METHANE PHYSISORPTION CAPACITY OF AMINOPROPYL-FUNCTIONALIZED MCM-41

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ABSTRACT

The increasing concentration of greenhouse gases in the atmosphere, particularly carbon dioxide (CO_2), poses global challenges to climate [1]. Effective capture and storage (and possibly reutilization) of this gas are critical for mitigating climate change [2]. This study explores the role of water molecules in the physisorption processes of CO_2 and CH_4 within mesostructured silica-based materials, by using MCM-41 as prototypical model. Following the previous investigations of the research group performed in the absence of humidity [3], the interactions between water, the sorbate molecules and the material surface has been studied as essential for optimizing the performance of these materials in real-world applications. A series of Grand canonical Monte Carlo (GCMC) and Molecular Dynamics (MD) simulations have been performed on both the bare material and the aminopropyl-functionalized version of one MCM-41 sample, at different relative humidity levels (5%, 10%, and 15% RH). The study was designed to assess the adsorption behaviour of water alone, and its impact on the adsorption capacities of CO_2 and CH_4. The GCMC methodology was applied to identify the correct amount of gas molecules at equilibrium under the given conditions of humidity, temperature and pressure, then, MD simulations were used to recover time evolution and calculate the diffusion coefficients, beside the other observables of interest, such as, radial density profiles and radial distribution function, adsorption capacity, and microscopical details about molecules interactions and spatial arrangement. The results demonstrated that the bare MCM-41 exhibited a significantly higher water adsorption capacity when compared to APS-Meso-3.4, primarily due to the reduced number of silanol groups on the material surface after functionalization. As humidity increased, water molecules formed clusters, which influenced the spatial distribution and interaction dynamics of CO_2 and CH_4 within the material pores. Notably, CO_2 displayed a greater affinity for adsorption than CH_4, with a marked increase in CO_2 capacity at low humidity levels, while higher humidity conditions led to a decrease in adsorption capacity. This research highlighted the critical interplay between water and gas adsorption in mesoporous materials, providing valuable insights into the mechanisms governing physisorption processes. The findings lay a solid foundation for future studies aimed at enhancing the efficiency of these materials for CO_2 capture.

REFERENCES

[1] S. C. Sherwood, M. J. Webb, J. D. Annan, K. C. Armour, P. M. Forster, J. C. Hargreaves, G. Hegerl, S. A. Klein, K. D. Marvel, E. J. Rohling, M. Watanabe, T. Andrews, P. Braconnot, C. S. Bretherton, G. L. Foster, Z. Hausfather, A. S. von der Heydt, R. Knutti, T. Mauritsen, J. R. Norris, C. Proistosescu, M. Rugenstein, G. A. Schmidt, K. B. Tokarska, M. D. Zelinka. An Assessment of Earth's Climate Sensitivity Using Multiple Lines of Evidence. Advancing hearth and space sciences, 2020 volume 58.
[2] D. S. Marlin, E. Sarron, O. Sigurbjörnsson. Process Advantages of Direct CO2 to Methanol Synthesis. Frontiers in Chemistry, 2018 Volume 6.
[3] P. Carta, M. A. Scorciapino. Surface Heterogeneity Affects Adsorption Selectivity for CO2 Over CH4 in Bare Mesostructured Silica with 2D Hexagonal Symmetry and Different Pore Size. Advanced Materials Interfaces, 2023 Volume 10.

P073: PHOTOSENSITIZERS FOR ADDITIVE MANUFACTURING OF CERAMIC MATERIALS

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ABSTRACT

Ceramic materials are being used in machines, electronics, semiconductors and aerospace applications due to their high hardness, high strength, chemical stability and high-temperature performance.[1] However, the outstanding hardness and strength of ceramic materials also make it difficult to shape and process ceramic parts.

Additive manufacturing techniques (also known as rapid prototyping and 3D printing) is a new fabrication approach that combines several fields of scientific knowledge, including computational techniques, material processing, mechanical processing, etc. The core concept of Additive Manufacturing (AM) is the fabrication of an object "from scratch": a component model is digitalized using computer-assisted design, from which a "sliced" data model is obtained.[2] A shaping machine is then used to "print" the component layer-by- layer to form a physical model. In theory, this process can be used to fabricate high-precision components using any material in arbitrary shapes, without any constraints in shape or feature.

Vat photopolymerization works by the principle of curing a photopolymer contained in a vat through light, layer-by- layer, to develop a 3D object. One of the main disadvantage is the limitation of being based on hazardous photoinitiator. To deal with this problem, a three-component system of the sensitizer/donor/acceptor type can be used.[3] In this work I propose some molecules and monomers that seems appear good candidates for this purpose since they presents many of the required characteristics to implement the system mentioned above.

REFERENCES

[1] R.B. Osman, A. J. van der Veen, D. Huiberts, D. Wismeijer, *Journal of the Mechanical Behavior of Biomedical Materials*, 75 (2017), 521-528.
[2] R. He, *Ceramics International*, 11 (2017), 135.
[3] Dadashi-Silab, S. Doran, Y. Yagci, *Photoinduced Electron Transfer Reactions for Macromolecular Syntheses*, Chem. Rev., 116, (2016) 10212-10275.

P074: PURIFICATION OF CROCIN-I FROM SAFFRON EXTRACT BY MEANS OF MULTICOLUMN COUNTERCURRENT SOLVENT GRADIENT PURIFICATION

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ABSTRACT

Saffron, the dried stigma of *Crocus Sativa L.,* has been plenty used in traditional medicine since is a great source of bioactive compounds. The most abound ingredients are a group of carotenoid-glycosyl- esters, that are known as crocins [1].

The types and number of sugar moieties vary among the different crocins, since their content is manly influenced by external factor as country origin, climate, storage conditions of saffron and other aspect in the and other aspects of agricultural production.

Among the crocins present in saffron extract, crocin-I has generated more and more attention due to its benefits for neurological, autoimmune, cardiovascular diseases and as anti-cancer agents.

The large-scale purification of this compounds is manly based on single column preparative liquid chromatography. However, this technique suffers from several drawbacks such large use of organic modifier and a labor-intensive procedure. Moreover, single column purification suffers from a purity-yield tradeoff, this means that in order to obtain a very pure product it is necessary to collect a very narrow collection window, since enlarging it would also collect some of the impurities that coelute with the target, lowering the purity value [2]. To overcome this problem instead of running more than one purification a possible strategy is to use a multicolumn continuous process.

In this work the Multicolumn Countercurrent Solvent Gradient Purification (MCSGP) has been used to purify crocin-I from a saffron extract. This technique, vastly used for biomolecules purification such as peptides, oligonucleotides and antibodies, allows to enrich the product target by recycling the side fractions contain also some of the impurities [3].

Furthermore, since the process is totally automated makes the process more robust, increasing also the productivity and environmental sustainability by decreasing the solvent consumption. Moreover, in this work the greenness of the process is also enhanced by the use of ethanol as organic modifier.

REFERENCES

[1] Hosseinzadeh, H., & Nassiri-Asl, M. (2013). Avicenna's (Ibn Sina) the canon of medicine and saffron (Crocus sativus): A review. In *Phytotherapy Research* (Vol. 27, Issue 4, pp. 475–483).

[2] de Luca, C., Felletti, S., Lievore, G., Chenet, T., Morbidelli, M., Sponchioni, M., Cavazzini, A., & Catani, M. (2020). Modern trends in downstream processing of biotherapeutics through continuous chromatography: The potential of Multicolumn Countercurrent Solvent Gradient Purification. In *TrAC - Trends in Analytical Chemistry* (Vol. 132).

[3] Luca, C. de, Felletti, S., Lievore, G., Buratti, A., Vogg, S., Morbidelli, M., Cavazzini, A., Catani, M., Macis, M., Ricci, A., & Cabri, W. (2020). From batch to continuous chromatographic purification of a therapeutic peptide through multicolumn countercurrent solvent gradient purification. *Journal of Chromatography A*, *1625*.

P075: DEVELOPMENT OF CONJUGATED TERPHENYL-BASED POROUS POLYMER FOR VISIBLE LIGHT-DRIVEN ORGANIC TRASFORMATIONS

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ABSTRACT

Porous Organic Polymers (POPs), have recently emerged as a powerful platform for heterogeneous photocatalysis. This class of porous materials feature large pores, high specific surface areas, good stability and robustness in various solvents, which are favourable for mass transfer, providing more active sites, allowing catalyst recyclability.[1] Moreover, the catalytic power of POPs can be fine tuned by modulating electronic properties of monomers and pore structures of the material, making these photocatalysts very attractive for photocatalytic applications. As a sub-class of POPs, Conjugated Porous Polymers (CPPs), thanks to their extended conjugation, exhibit a strongest light-harvesting ability and smaller energy gap between excited states ($\Delta E_{S\text{-}T}$) compared with traditional small-molecule photosensitizers. In this context, a few examples of conjugated polymers have been proven to serve as triplet photosensitizers to promote the $^1O_2$ production[2] or various types of cross-coupling reactions.[3] In this study, we report a synthesis of *p*-terphenyl-based CPP through a polycondensation reaction between 4,4"-diamino-p-terphenyl and cyanuric chloride. The morphology of the resulting polymer was assessed through SEM analysis, which highlighted the macroporous structure of the material. In addition the photochemical properties were evaluated trough UV-Vis DRS, DFT calculations and cyclic voltammetry. Compared to *p*-terphenyl photosensitizer (λ_{max} = 283 nm), Terphenyl-CPP exhibit a broad absorption band red-shifted (λ_{max} = 380 nm) and a bandgap E_g = 3.12 eV which make this material able to absorb the visible light (400-800 nm). Once the synthesis and characterization of the novel material were completed, the catalytic performance were evaluated. Terphenyl-CPP was demonstrated to be a promising heterogeneous photocatalyst for visible-light-promoted organic transformations, including selective oxidation of sulfides in water/ethanol and cross dehydrogenative coupling between N-aryl glycines and indoles for the synthesis of non-proteinogenic α-amino acids, affording the desire products in good or excellent yields under mild conditions.

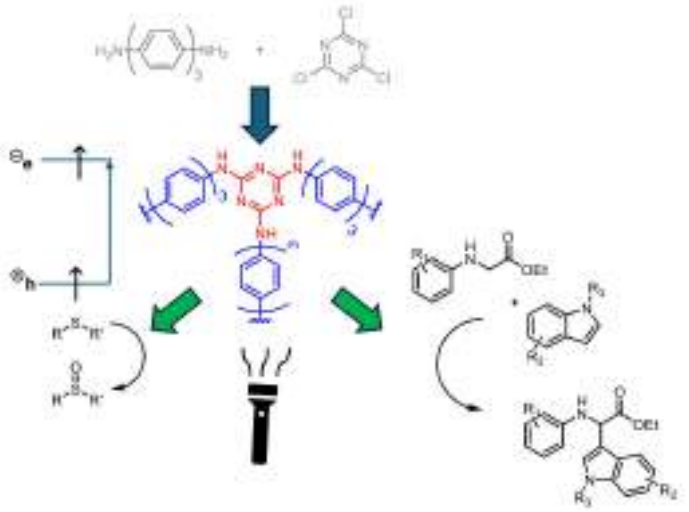

Figure 1. Synthesis and application of Terphenyl-CPP.

REFERENCES

[1] Zhang, T.; Xing, G.; Chen, W.; Chen, L. *Mater. Chem. Front.* **2020**, *4* (2), 332–353.
[2] Zhu, S.-S.; Liu, Y.; Chen, X.-L.; Qu, L.-B.; Yu, B. *ACS Catal.* **2022**, *12* (1), 126–134.
[3] Wu, W.; Mao, D.; Xu, S.; Kenry; Hu, F.; Li, X.; Kong, D.; Liu, B. *Chem* **2018**, *4* (8), 1937–1951.

P076: BLOCK TERM DECOMPOSITION: A BREAKTHROUGH IN HYPERSPECTRAL IMAGE ANALYSIS

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ABSTRACT

Tensor decomposition methods have long been recognized as robust tools in chemometrics, providing effective approaches for analysing complex data structures [1]. In hyperspectral imaging, where the simultaneous exploration of spatial and spectral domains is essential, techniques such as Canonical Polyadic Decomposition (CPD) and Tucker decomposition [2] are widely used. However, CPD's strict rank-1 constraint on each factor can limit its applicability, while Tucker decomposition offers greater flexibility but is affected by rotational ambiguity. Block Term Decomposition (BTD) [3] provides a valuable middle ground. Specifically, the rank-(L_r,L_r,1)-BTD variant imposes a rank-1 constraint on one factor while allowing higher ranks for the other two factors (**Figure 1**). This approach retains the uniqueness of CPD while better capturing complex spatial structures associated with a single spectral signature. This makes rank-(L_r,L_r,1)-BTD particularly suited for hyperspectral image analysis, addressing scenarios with minor components, components with similar spatial distributions but distinct spectral signatures, and vice versa. In this work, we focus on determining the subfactors L_r, a critical step for the effective application of this method. We investigate the use of rank-(L_r,L_r,1)-BTD for analysing benchmark hyperspectral imaging datasets, including chemical mixtures, biological fluids, and remote sensing images. These datasets span multiple spectroscopic techniques, such as UV-Vis, NIR, Raman. The results highlight the potential for rank-(L_r,L_r,1)-BTD method in hyperspectral image analysis, offering valuable insights into the efficacy of tensor-based decomposition methods for addressing the significant challenges posed by such data.

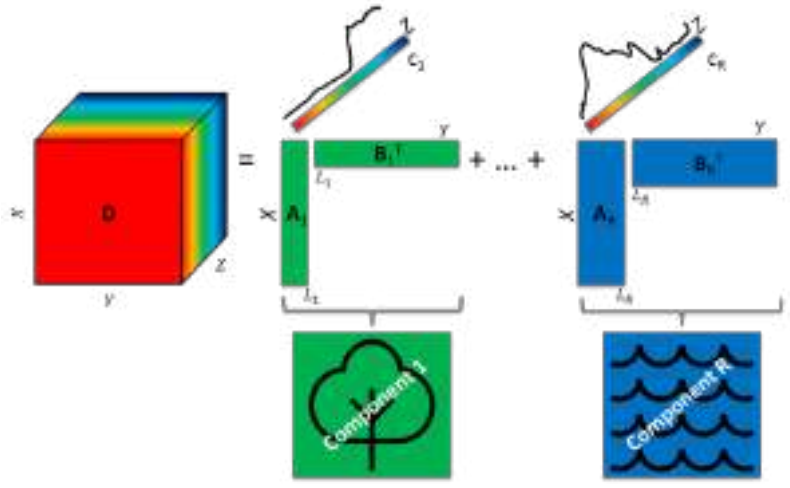

Figure 1. Hyperspectral data cube **D** (X × Y × Z) is decomposed as the sum of outer product of a component matrix, resulting from the product of the two spatial dimension factor matrices **A** (X × L_r), **B** (L_r × Y) of equal rank ≠1, and a vector **c** of length Z (rank = 1, which is the spectral factor).

REFERENCES

[1] E. Acar, Y. Bülent, IEEE transactions on knowledge and data engineering, 2008, 21, 6-20.
[2] T.G. Kolda, W.B. Bader, SIAM review, 2009, 51, 455-500.
[3] L. De Lathauwer, SIAM Journal on Matrix Analysis and Applications, 2008, 30, 1033-1066.

P077: MICROFLUIDIC OPTIMIZATION OF LIPID NANOPARTICLES FOR CRISPR/CAS9 DELIVERY TO *EX-VIVO* STEM CELLS

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ABSTRACT

Gene therapy has revolutionized traditional therapeutic strategies, enabling novel therapeutic approaches for previously untreatable genetic diseases. It is now widely applied to various pathologies, including cancer, autoimmune, and cardiovascular disorders. CRISPR/Cas9 (complexed with a sgRNA in the Ribonucleoprotein complex, RNP) is a cutting-edge tool in this field, facilitating precise genome editing for long-term expression or gene knockdown. Developing scalable, non-viral delivery systems such as nanoparticles for CRISPR/Cas9 delivery represents a significant advancement for gene therapy [1,2].

This study optimized a microfluidic method for formulating lipid nanoparticles (LNPs) to encapsulate a model enzyme, β-glucosidase, which mimics the size (135 kDa) and charge of the RNP complex. Key formulation parameters, such as enzyme-to-lipid ratio, were fixed, while lipid composition, total flow rate (TFR), and flow rate ratio (FRR) were varied. The study synthesized and analyzed 24 empty LNPs using cholesterol, DSPC or DPPC, and DOPE in ethanol. From these, 16 promising formulations were selected for further analysis and used to encapsulate β-glucosidase. Only 9 out of 16 formulations resulted in monodispersed LNPs after enzyme encapsulation.

These formulations that were able to load the enzyme were then evaluated for cell uptake and viability on hematopoietic stem cells. The SC formulation (cholesterol 50%, DSPC 25%, DOPE 25%) demonstrated the highest uptake (~20%) when dosed at 100 µg/mL, with limited toxicity. To improve encapsulation efficiency and promote interaction with cell membranes, the cationic lipid DOTAP was added at various molar percentages to SC. SC DOTAP 5% and 10% formulations (FRR 1:1, TFR 6 mL/min) achieved an encapsulation efficiency of 4% and 11%, respectively. Moreover, SC DOTAP 5% exhibited the highest cell uptake (87%) at 100 µg/mL while maintaining a good safety profile.

This lipid formulation, characterized by high uptake and safety, holds promise for scaling up via microfluidics. Future work will focus on RNP-loaded LNPs to evaluate their physicochemical properties and in vitro efficacy.

REFERENCES

[1] Kim, M.; Hwang, Y.; Lim, S.; Jang, H.-K.; Kim, H.-O. Advances in Nanoparticles as Non-Viral Vectors for Efficient Delivery of CRISPR/Cas9. *Pharmaceutics* **2024**, *16*, 1197, doi:10.3390/pharmaceutics16091197.

[2] Zhang, T.; Ding, J.; Lv, Q.; Zhao, M.; Liu, Y.; Wang, Q.; Chen, Y.; Zhao, H.; Ren, H.; Jiang, W.; et al. Strategies for Organic Nanoparticles Delivering CRISPR/Cas9 for Cancer Therapy: Challenges and Breakthroughs. *Materials & Design* **2024**, *244*, 113097, doi:10.1016/j.matdes.2024.113097.

P078: PRESSURE-INDUCED STRUCTURAL VARIATIONS AND MECHANICAL BEHAVIOR OF SILICATE GLASSES: ROLE OF ALUMINUM AND SODIUM

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ABSTRACT

Aluminosilicate glasses are known for their broad range of composition-dependent properties, making them indispensable for applications across diverse fields. The inclusion of aluminium in these glasses enhances several key properties, including chemical durability, viscosity, and thermal stability, while also improving mechanical robustness by reducing the tendency toward devitrification and minimizing thermal expansion [1]. Furthermore, the presence of alkali cations like sodium influences the configurational connectivity of the aluminosilicate network, which in turn affects the packing density and overall physico-chemical properties of the glass. This dual contribution enables fine-tuning of glass characteristics to meet specific application demands.
In recent studies, it has been shown that applying high pressure during glass production has a significant impact on glass structure and mechanical properties. Techniques such as hot compression annealing, where glass is subjected to high pressure near its glass transition temperature (Tg), have been demonstrated to induce permanent densification, leading to alterations in both the atomic structure and macroscopic mechanical performance. This pressure-induced densification affects various mechanical properties such as hardness, toughness, and crack resistance, making it a powerful tool for designing glasses with enhanced structural attributes [2].
In this work, we used classical molecular dynamics (MD) simulations to explore the impact of pressure-induced densification on two specific glass compositions: an albite-like glass (12.5% Na_2O, 12.5% Al_2O_3, and 75% SiO_2) and a sodium silicate glass with equivalent sodium content (12.5% Na_2O, 87.5% SiO_2). These compositions were selected due to their common industrial applications and their distinct structural roles of sodium and aluminum. In albite glass, sodium ions act as charge compensators for AlO_4^- units, while in sodium silicate glass, sodium serves as a network modifier, creating non-bridging oxygens that disrupt the glass network connectivity. By analyzing these contrasting roles, we aim to gain a deeper understanding of the effects of sodium and aluminum on glass densification and related mechanical properties.
Our simulations focused on the structural and mechanical alterations resulting from densification under 1.5 GPa pressure. We calculated several elastic properties (Young's, Shear, and Bulk moduli, and Poisson ratio) and conducted mechanical tests such as uniaxial tensile and hydrostatic compressive loading to evaluate changes in strength, fracture behavior, and elasticity. These simulations also examined atomic-scale modifications, including changes in bond lengths, ring configurations, and oxygen coordination, providing insight into how these structural features correlate with macroscopic properties like toughness and ductility. By comparing albite and sodium silicate glasses, this study sheds light on the complex interplay between composition, structural response to pressure, and mechanical performance, offering guidance for designing advanced glass materials with tailored properties for demanding technological applications.

REFERENCES

[1] J. Arndt, F. Haberle, Thermal expansion and glass transition temperatures of synthetic glasses of plagioclase-like compositions, Contrib. Mineral. Petrol. 39 (1973) 175–183, https://doi.org/10.1007/BF00375739.
[2] M. Guerette, M.R. Ackerson, J. Thomas, F. Yuan, E. Bruce Watson, D. Walker, L. Huang, Structure and properties of silica glass densified in cold compression and hot compression, Sci. Rep. 5 (2015) 15343, https://doi.org/10.1038/srep15343.

P079: DATA FUSION FOR FOOD AUTHENTICITY AND VALORIZATION: TWO CASES OF STUDY

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ABSTRACT

Food fraud is a significant food safety problem [1] and to contrast such practice, robust authentication methods are needed. For this purpose, two main categories of analysis methods can be used: (i) targeted approach that focuses on specific markers known a priori, using reference standards and databases and (ii) untargeted approach that aims to collect as much information as possible, using fingerprinting and machine learning techniques to develop discrimination and classification models. In this study the untargeted approach was applied to two cases of study: potatoes labelled "Patata di Montese" with "Mountain product" denomination and Balsamic Vinegar of Modena PGI. In the first case, the aim was to characterize the metabolomic pattern by means of Liquid-Chromatography-High-Resolution-Mass-Spectrometry (LC-HRMS) and Nuclear Magnetic Resonance (NMR) and to find biomarkers of the "Patata di Montese" samples. The complex metabolomics big datasets generated by LC-HRMS were analyzed using the ROI-MCR strategy [2], involving the Region of Interest (ROI) procedure for data filtering, compression, preprocessing, and storage steps. Multivariate Curve Resolution-Alternating Least Square (MCR-ALS) was then applied to the previously MS ROI preprocessed datasets to resolve the elution profiles and spectra fingerprints of the chemical constituents. The resolved features were putatively identified using different reference spectral libraries. The complex spectroscopic dataset was divided into several intervals and on each interval a MCR model was built. At the end, resolved NMR signals were obtained. In the second case, the aim was to detect synthetic caramel in vinegar samples by means of Gas-Chromatography-Mass-Spectrometry (GC-MS) and excitation-emission spectroscopy (EEM). Both techniques result in three-dimensional datasets (i.e. samples x emission wavelengths x excitation wavelengths for fluorescence spectroscopy; samples x retention time x mass spectra for GC-MS) that require the application of appropriate data analysis techniques. In the case of fluorescence, PARAFAC [3] was applied to resolve and quantify fluorophores related to the presence of caramel. For the GC-MS analysis, PARADISe software [4] was used for the resolution, integration and identification of analytes characterising the aroma of vinegar samples. Just as humans use multiple senses to assess food quality, combining data from various sources enhances the accuracy of food authentication assessment. In both cases two techniques were used for the analysis of the samples and a mid-level data fusion was performed. During mid-level data fusion, the resolved features were merged and a single model for each case was built.

REFERENCES

[1] Medina, S.; Perestrelo, R.; Silva, P.; Pereira, J.A.M.; Câmara, J.S. Current Trends and Recent Advances on Food Authenticity Technologies and Chemometric Approaches. Trends Food Sci. Technol. 2019, 85, 163–176.
[2] M. Perez-Cova, C. Bedia, D. R. Stoll, R. Tauler, J. Jaumot. Chemometrics and Intelligent Laboratory Systems, 215 (2021), 10433.
[3] R., Bro, Chemometrics and Intelligent Laboratory Systems 1997, 38, 149-171.
[4] L. G., Johnsen, P. B., Skou, B., Khakimov, R., Bro, Journal of Chromatography A 2017, 1503, 57-64.

P080: NOVEL MATERIALS FOR SYNTHETIC PROSTHESIS FOR THE TREATMENT OF CHRONIC CORNEAL EDEMA

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ABSTRACT

Corneal diseases, including keratoconus, corneal edema and leukomas, are the leading cause of blindness worldwide [1]. The corneal endothelium, which is the innermost layer of the cornea, is the tissue mainly affected by corneal edema. Since human corneal endothelial cells show no ability to proliferate and regenerate *in vivo*, their damage can lead to loss of corneal clarity and blurred vision. Corneal transplantation is currently considered the mainstay of treatment for patients with various forms of endothelial dysfunction; however, it is not always accessible, effective or practical. Additionally, the demand for donor corneas far surpasses their availability, particularly in disadvantaged countries [2]. Last, there is an urgent need to find alternatives for patients who are at risk of keratoplasty failure. In this regard, a synthetic endothelial prosthesis, EndoArt® (EyeYon Medical, Ness Ziona, Israel) [3] has been patented and already successfully implanted to restore visual function. This synthetic tissue is made of a transparent, flexible and biologically compatible copolymer of hydroxyethyl methacrylate and methyl methacrylate (Figure 1). As known, acrylic materials are widely and commonly used for the production of commercial ophthalmic implants, such as hydrophilic intraocular lenses. In detail, EndoArt® is a durable, reproducible, easily removable or replaceable, biocompatible and biostable device and, due to its nonbiologic nature, does not require any immunosuppressive treatment. On the other hand, problems of non-adhesion to the stromal surface were found in most cases, requiring a second surgery to improve contact between the device and the inner corneal wall. Therefore, further solutions made of acrylate-based copolymers could be potentially suitable to obtain corneal devices capable of overcoming the EndoArt® limitations. In the present study, ethylene and methyl acrylate copolymers, or ethylene and butyl acrylate copolymers, with different relative compositions, were considered. In detail, films obtained by compression moulding were characterized from the molecular, thermal, mechanical and surface wettability point of view. The biocompatibility was also assessed through *in vitro* cytotoxicity tests, using human corneal fibroblasts. From the results obtained, it can be assessed that these materials can be used for all the applications were softness, flexibility and polarity are required and, thanks to their transparency, they turned out to be good candidates for applications as non-cellular corneal substitute.

Figure 1. EndoArt® (EyeYon Medical, Ness Ziona, Israel).

REFERENCES

[1] The Lancet Global Health, 2021, 9, E130-43.
[2] Holland et al., Frontiers in Medicine, 2021, 8, 770780.
[3] Auffarth et al., Cornea, 2021, 40, 1633-1638.

P081: DEVELOPMENT OF RIBONUCLEASE TARGETING CHIMERAS (RIBOTACS) FOR THERAPEUTIC APPLICATIONS

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ABSTRACT

The renewed interest in RNA as a drug target, fuelled by fundamental insights into its structural and functional complexity, has broadened the range of therapeutic strategies to encompass non-coding RNAs (ncRNAs) such as miRNAs, snRNAs, and rRNAs as potential novel targets. This "RNAissance" has spurred intense medicinal chemistry efforts to develop selective and potent RNA therapeutics.[1]
RIBOnuclease TArgeting Chimeras (RIBOTACs) represent a cutting-edge approach, based on small molecule chimeras that act by chemically bringing RNA targets into proximity with a RNA effector, the endogenous Ribonuclease L (RNAse L) to degrade targeted RNAs (**Figure 1**). These chimeric molecules comprise three key elements: an RNA-binding domain that selectively targets a specific RNA of interest (ROI), and a recruitment module that binds RNAse L, connected via a linker.[2] RIBOTAC catalytic mechanism allows for the iterative degradation of disease-relevant RNAs, such as pre-miR-515, miR-372, and miR-21, which are implicated in tumours, mainly breast cancers and gastric carcinomas, without depleting the RIBOTAC itself.[3]
Our project focuses on the rational design and synthesis of a library of high-affinity, selective RNA binders to be used for RIBOTAC development Structure-activity relationship (SAR) studies will allow to select the best RNA binders, which will be then linked to the RNAse L recruitment module via different linkers. Ultimately, this work aims to develop novel and potent RNA therapeutics with significant implications for treating RNA-driven diseases.

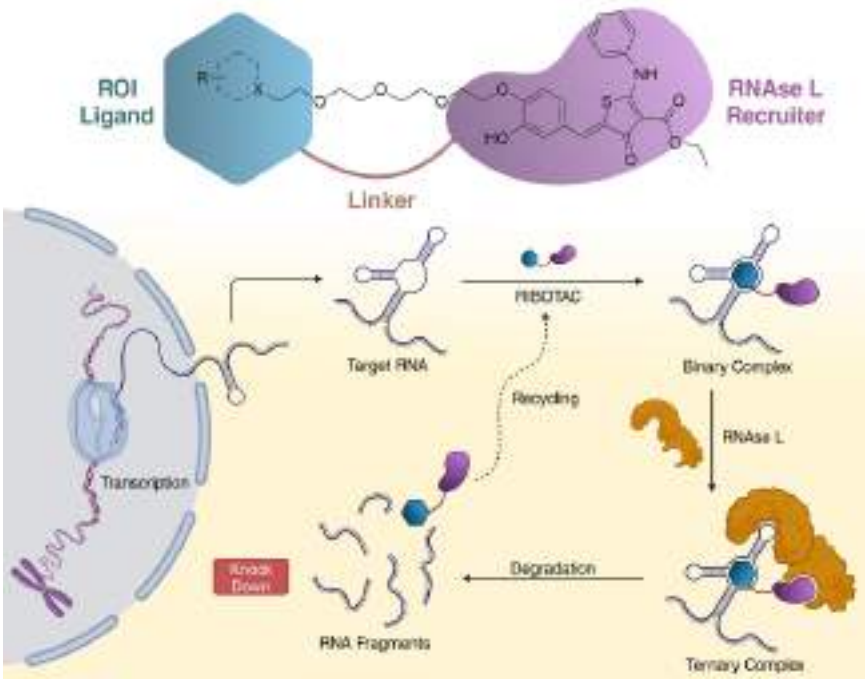

Figure 1. RIBOTACs mechanism of action.

REFERENCES

[1] Jones, C.H.; et al. *npj Genom. Med.* 9, 2 (**2024**).
[2] Costales, M. G.; et al. *J Med Chem*. 63, 8880-8900 (**2020**).
[3] Tong, Y.; et al. *Nature* 618, 169–179 (**2023**).

P082: DESIGN AND SYNTHESIS OF PROTACS (PROTEOLYSIS TARGETING CHIMERAS) AS INNOVATIVE DRUGS FOR WEST NILE INFECTIONS

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ABSTRACT

In recent years, West Nile virus (WNV) and other vector-borne viruses, belonging to the Flaviviridae family such as Zika and Dengue, have begun to expand very rapidly.
Initially, West Nile was located only in Africa and Asia, but global megatrends, like uncontrolled urbanization, climate change and increased intercontinental travel, promote the spread of flaviviruses in America and Europe too. Specifically, in Italy, the Emilia-Romagna region has been called a "virus hotspot in Europe" due to its lagoon territory and humid climate where the vector is able to replicate very rapidly. This virus can cause several symptoms like flu, papular macular rash, Guillain-Barré syndrome, encephalitis or meningitis, movement disorders and no medical treatments are currently available. In view of that, and with the aim to limit the likelihood of the development of a new epidemic and prevent the increase of diseases attributable to this family of viruses, there is an urgent need to develop new selective drugs. To date, most of the drugs are small molecules that work primarily via occupancy-driven pharmacology as mode of action (MoA), but recently a new innovative technology called Proteolysis Targeting Chimeras (PROTACs) has emerged[1]. This new approach is based on the use of the endogenous ubiquitin-proteasome system to induce protein degradation. PROTACs are heterobifunctional small molecules consisting of two ligands, one responsible for recruiting the E3 ligase, while the other one with affinity for the protein of interest, joined by a suitable linker, essential for the pharmacokinetics and pharmacodynamics properties. The aim of the project is the development of new PROTACs targeting the viral Serine Protease NS2B-NS3[2], with NS3 having NS2B as a cofactor. In addition, NS3 has the 5′-RNA triphosphatase activity (5′-RTPase), nucleoside triphosphatase (NTPase)[3], and helicase activity essential for viral replication, making it an interesting antiviral target. Furthermore, this protease is not present in mammalian host, its structure and mechanism are conserved in different arboviruses (DENV, WNV and ZIKA) and it is genetically validated. Additionally, there are different crystallographic structures of the NS2B-NS3 complex.
In conclusion, our final PROTACs might represent a new avenue to target flavivirus infectious.

Figure 1. WNV infection cycle and PROTACs as pharmacological treatment.

REFERENCES

[1] Salerno, A. et al. *J. Med. Chem.* **2022**, *65*, 9507-9530.
[2] Petersen L.R. et al *Emerg Infect Dis*. **2001**, *7*, 611-614.
[3] Changsuek Yon et al *JBC* **2005**, *280*, 29, 27412-27419.

Acknowledgment: Fondazione Flaminia, Ravenna.

P083: SYNTHESIS OF BIOBASED MONOMERS AND POLYMERS

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ABSTRACT

As fossil sources depletion and pollution are posing severe drawbacks to the polymer industry, the need for new pathways for the production of materials by renewable and sustainable means arises. The aim of the project is producing bio-based monomers and, subsequently, the corresponding bio-based polymers. The focus is on polyolefins and epoxy resins. The substrates come from the upgrading of agricultural and forestry industries waste streams. Those are mainly vanillin, guaiacol, furfural and glycerol, which are all potentially renewable and for which it is expected an increase in production in the near-term future[1-3]. In the case of olefins, their production is aimed towards Atom Transfer Radical Polymerization (ATRP). The technique allows precise tailoring of chain length and molecular weight distribution by means of a reversible deactivation equilibrium mediated by a transition metal salt complex. The technique is to be considered environmentally benign as it operates in mild conditions and is able to achieve control even at catalyst loadings as low as ppm levels[4]. 4-Vinyl Guaiacol Acetate (4-VG-Ac), Vanillin MethAcrylate (VMA) and Vanillin Ethylene MethAcrylate (VEMA) were successfully produced from vanillin and polymerized in a controlled fashion by SARA ATRP. Studies on their metal-free ATRP are being performed to increase process sustainability. As bisphenols are being banned by the European Union due to its endocrine disrupting activity, there is need for sustainable and lower toxicity alternatives. Guaiacol is the ideal substrate to upgrade, as it was demonstrated that the higher degree of substitution of the aromatic ring results in a decrease in toxicity by various orders of magnitude[5]. Various reaction pathways were tested on laboratory scale. Production of 2-Methoxy Hydroquinone (MHQ) was performed by Dakin oxidation of vanillin, affording minimal waste production. Guaiacol condensation by oxidative coupling into the corresponding triphenylene was performed, albeit at non-satisfactory conversion values. Condensation studies performed on furfural and furfural derivatives have been unsuccessful. Studies on guaiacol dimerization into bisguaiacols by electrophilic aromatic substitution reactions are ongoing. Upscaling is planned to afford the quantities required for mechanical testing. The corresponding bi-component resins will be tested as binders in mortars for the construction sector and in epoxy/graphite composites in bipolar plates for fuel cells, aimed towards sustainable hydrogen production.

REFERENCES

[1] F. Mundo, S. Caillol, V. Ladmiral, M.A.R. Meier, On Sustainability Aspects of the Synthesis of Five-Membered Cyclic Carbonates, ACS Sustainable Chem. Eng. 12 (2024) 6452–6466. https://doi.org/10.1021/acssuschemeng.4c01274.

[2] J. Zakzeski, P.C.A. Bruijnincx, A.L. Jongerius, B.M. Weckhuysen, The Catalytic Valorization of Lignin for the Production of Renewable Chemicals, Chem. Rev. 110 (2010) 3552–3599. https://doi.org/10.1021/cr900354u.

[3] A. Gandini, T.M. Lacerda, A.J.F. Carvalho, E. Trovatti, Progress of Polymers from Renewable Resources: Furans, Vegetable Oils, and Polysaccharides, Chem. Rev. 116 (2016) 1637–1669. https://doi.org/10.1021/acs.chemrev.5b00264.

[4] K. Matyjaszewski, Atom Transfer Radical Polymerization (ATRP): Current Status and Future Perspectives, Macromolecules 45 (2012) 4015–4039. https://doi.org/10.1021/ma3001719.

[5] Y. Peng, K.H. Nicastro, I. Epps Thomas H., C. Wu, Methoxy groups reduced the estrogenic activity of lignin-derivable replacements relative to bisphenol A and bisphenol F as studied through two *in vitro* assays, Food Chemistry 338 (2021) 127656. https://doi.org/10.1016/j.foodchem.2020.127656.

P084: IMPROVED LEATHER PROPERTIES THROUGH ULTRASONICALLY-PRODUCED HYDROXYAPATITE/β-CYCLODEXTRIN COMPOSITES

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ABSTRACT

One of the main problems associated with the tanning industry is that significant amounts of hazardous substances are released into the environment causing problems for the ecosystem and human health [1].
The development of non-toxic and biodegradable additives that guarantee the quality performance of durable and functional leather without contaminating the environment is therefore crucial.
In this work, ultrasound, a green and clean technology, was used for the synthesis of β-cyclodextrins/hydroxyapatite-based composites to improve the leather quality [2,3]. The use of ultrasound to reduce the size of the hydroxyapatite particles (sono-deagglomeration) was found to be effective, as was the use of cyclodextrin to increase the stability and solubility of the nano-HAp particles. The composites were chemically and structurally characterised by ATR-FTIR, TG/DTG, XRD and SEM analyses and showed antibacterial activity and no cytotoxicity. The interaction of the composites with collagen was demonstrated by MHT method, micro-DSC and SEM.
The best composite was tested on a pilot scale, showing improved leather properties compared to commercial products in terms of colour brightness, colour fastness, grain fullness, thickness, thermal stability, and breathability. This sustainable approach is attractive as it demonstrates the value of composites as safe and sustainable tanning additives.

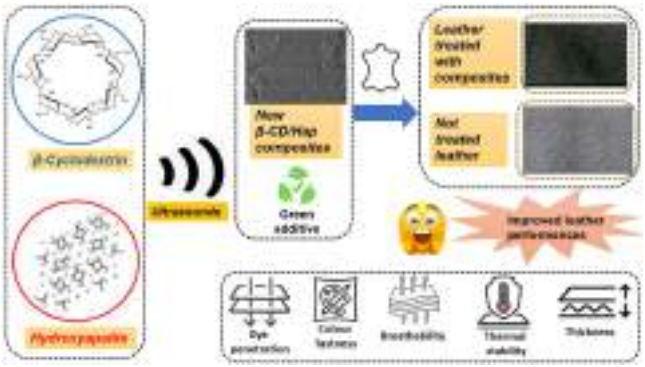

Figure 1. A schematic representation of the process.

REFERENCES

[1] K. J., R.C. Panda, V.K. M., Trends and advancements in sustainable leather processing: Future directions and challenges—A review, *J. Environ. Chem. Eng.*, **2020**, *8*, 104379.
[2] C. Ingrao, E. Vesce, R.S. Evola, E. Rebba, C. Arcidiacono, G. Martra, R. Beltramo, Chemistry behind leather: Life Cycle Assessment of nano-hydroxyapatite preparation on the lab-scale for fireproofing applications, J. Clean. Prod., **2021**, *279*, 123837.
[3] N. Sharma, A. Baldi, Exploring Versatile Applications of Cyclodextrins: An Overview. *Drug Deliv.*, **2016**, *23*, 729–747.

P085: VOLATILOMICS, BREWING AND MULTIVARIATE STATISTICAL ANALYSIS: NEW INSIGHTS INTO THE PRODUCTION OF BEER

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ABSTRACT

Beer is one of the most popular beverages worldwide. The production of craft beer has increased dramatically in recent year, however, despite volatilomics [1] plays a significant role in food quality and authenticity assessment, only a reduced number of studies have afforded a rigorous evaluation of the aromatic profile of craft beer. The complex volatile profile of this product is influenced by both raw materials and brewing procedures with a variety of volatile compounds, including alcohols, esters, carbonyl compounds, sulfur compounds, and terpenes able to affect the flavor and taste of beer. In this study, a solid-phase microextraction (SPME)-GC-MS method was developed to study the volatile profile of four different craft beers, namely American IPA (**AI**) and Cream Ale (**CA**) (high fermentation beers), Vienna Lager (**VL**) and Bohemian Pilsner (**BP**) (low fermentation beers). The use of a 50/30 µm DVB/CAR/PDMS fiber exposed in the headspace above the sample for 20 min at 60 °C, allowed for the extraction of more than 59 compounds. Compound annotation was carried out by comparing: i) the experimental spectra with those stored in the NIST library, ii) the calculated Kovats indices with those reported in literature or stored in proprietary databases [2], iii) the injection of pure standards. Multivariate statistical analysis, namely principal component analysis proved to be useful in differentiating the beer samples (Fig. 1a and b) being the 74% of the variance explained by the first two PCs. As shown in Fig. 1, AI beers could be differentiated according to PC1, whereas PC2 was useful in discriminating CA from BP beers.

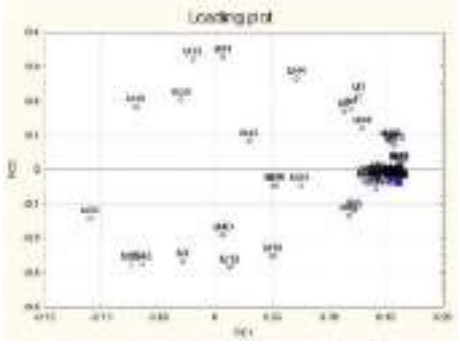

Figure 1a. Score plot

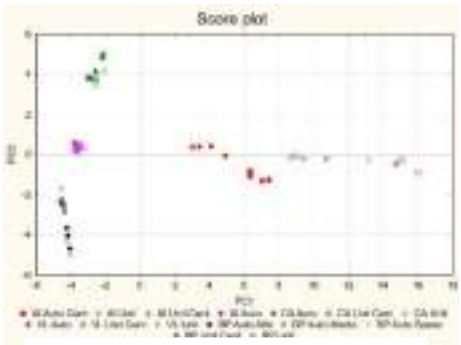

Figure 1b. Loading plot

The relationship between chemical compounds and fermentation in beer can be summarized as follows: i) esters (e.g. ethyl acetate, isoamyl acetate) impart fruity and floral notes, their production is favored by fermentations at higher temperatures (CA, AI), while cooler fermentations (VL, BP) make the beer cleaner; ii) alcohols (e.g. isobutyl alcohol) add aromatic complexity: they are mainly produced in CA and AI due to the high brewing temperatures, whereas they are reduced in VL; iii) terpenes and hop compounds (e.g. myrcene, linalool) come from the hops and can be altered by the fermentation process. The presence of complex esters and organic acids (e.g. ethyl isobutyrate) depends on both the type of yeast and fermentation conditions such as temperature and oxygenation; iv) other volatile compounds (e.g. 2-nonanone) are influenced by both maturation and the lagering process, which in lagers contributes to a 'cleaner' profile.

REFERENCES

[1] S. Giannoukos, A. Agapiou, B. Brkić, S. Taylor, Journal of Chromatography B, 1105 (2019) 136-147
[2] F. Bianchi, M. Careri, A. Mangia, M. Musci, Journal of Separation Science, 30 (2007) 563-572

P086: SYNTHESIS OF C-GLYCOSYL AMINO ACIDS *VIA* STEREOSELECTIVE GIESE ADDITION TO KARADY-BECKWITH ALKENE MEDIATED BY PHOTOCATALYSIS

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ABSTRACT

Based on the previous work reported by our group on the synthesis of C-glycosyl amino acids by photocatalytic Giese reaction[1], we envisaged the possibility of improving the selectivity of the reporting methodology by mean employing new acceptors, expanding the reaction scope to Levoglucosenone (LGO, a biobased product from cellulose processing), and improving the sustainability as well. Herein, we present a synthetic strategy to access C-glycosyl amino acids *via* Giese-type photocatalyzed reactions mediated by TADF (Thermally Activated Delayed Fluorescence) [2]. The stereoselective addition of *in situ* generated pyranosyl radical (glycosyl radicals and LGO derivative radicals) is fostered by a chiral dehydro-amino acid named Karady-Beckwith alkene. The resulting coupling adduct was obtained in high d.r. (>20:1) and good yield (62%) when the benzoyl protected galactosyl bromide is employed in DCM using 4CzIPN (TADF); whereas moderate reactivity was observed when levoglucosenone derivatives such as cyrene were employed (yield up to (55%)). Preliminary studies employing polymeric TADF photocatalysts POP (heterogeneous catalysis) reveal good reactivity, allowing for future exploration in this regard.

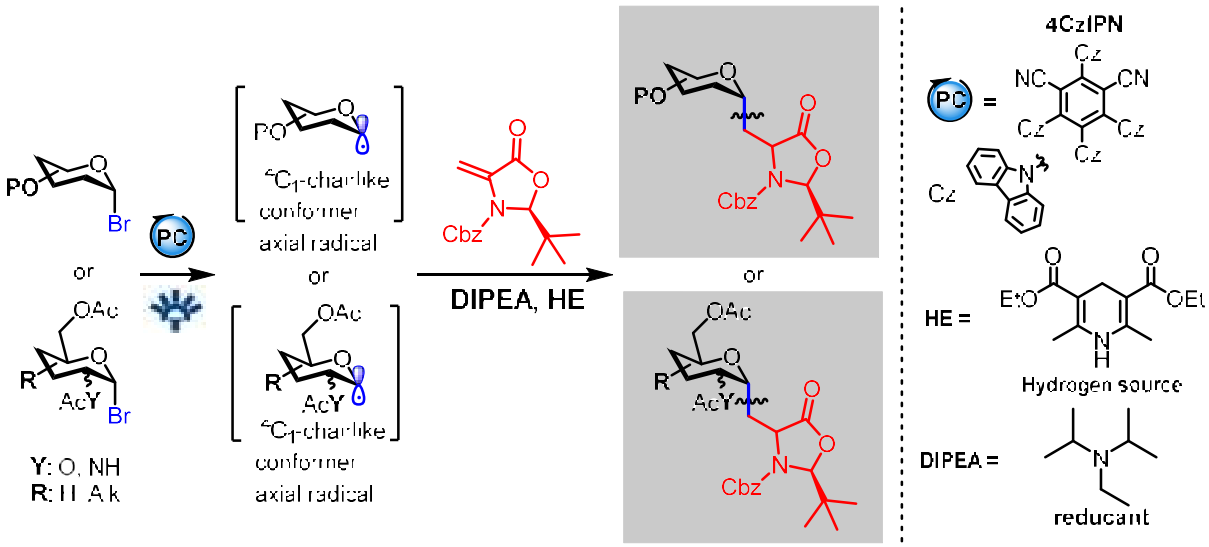

Fig. 1. *Radical addition promoted by 4CzIPN, in Giese-type reaction.*

References:

[1] G. Di Carmine et al., Org. Lett. **2023**, 25, 4862−4867
[2] Zeitler et al., J. Am. Chem. Soc. **2018**, 140, 45, 15353–1536

P087: NON-STEROIDAL FGF TRAPS EFFECTIVELY AND SELECTIVELY REDUCE THE GROWTH OF MULTIPLE MYELOMA IN MICE XENOGRAFT

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ABSTRACT

Fibroblast growth factors (FGFs) promote cell division and blood vessel formation in multiple myeloma (MM). Dysregulated secretion of FGFs leads to abnormal activation of the FGF receptor (FGFR), promoting the proliferation of different cancer cells and resistance to conventional therapies. While inhibition of FGFR at the kinase domain can produce undesired side effects such as hyperphosphatemia, an alternative approach to impair dysregulated FGFR activation is to sequester FGF from the extracellular environment through the so-called FGF traps. Although a protein-based FGF trap has progressed to clinical trials, the discovery and development of small-molecule FGF traps is still at the early development stage. In particular, a steroidal compound (NSC12) and its derivative had shown FGF-trap activity and anti-tumor effects in different animal models. On the other hand, investigations about structure-activity relationships (SARs) for this scaffold is hampered by the inherent challenges associated with the structural modification of the steroid nucleus. Thus, to facilitate a broader examination of the structural requisites for FGF binding and the inhibition of FGF/FGFR system signaling, we employed a scaffold hopping strategy to devise non-steroidal FGF traps. Different bioisosteric substitutions were assessed, comprising the biphenyl and the (phenyl)-naphthyl scaffolds, and more non-flexible analogs.
The optimized compounds demonstrated robust anti-tumor efficacy against MM cell lines as well as in primary cells derived from MM patients, significantly improving the survival of both Bortezomib-sensitive and resistant MM cells. These compounds significantly reduced the growth of MM tumor xenografts in mice without the hyperphosphatemic side effect observed after the treatment with FGFR tyrosine kinase inhibitors. These findings present a promising therapeutic avenue for relapsed/refractory MM patients and lay the groundwork for the development of novel FGF traps for clinical use in tumors where the FGF/FGFR system plays a crucial role.

REFERENCES

[1] R. Castelli et al. J. Med. Chem. 59 (2016) 4651-4663
[2] R. Castelli et al. Eur. J. Med. Chem. 221 (2021) 113529
[3] R. Ronca et al. Cancer Cell. 28 (2015) 225–239

P088: DIFFERENT STRATEGIES TO TARGET GSK3β AND FYN TO INVESTIGATE NEUROINFLAMMATION

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ABSTRACT

Dysregulation of protein kinases (PKs) in central nervous system (CNS) is implicated in numerous neurodegenerative diseases including Alzheimer's disease (AD)[1]. Among the several kinases in the system, GSK3β is considered a key player in the pathophysiology of tauopathies because of its involvement in all major hallmarks as protein misfolding, inflammation and synaptic dysfunction[2]. More recently FYN kinase has also emerged as an attractive therapeutic target not only for tau protein-related neurotoxic dysregulation, but also for its involvement in several proinflammatory pathways[3]. To better understand the involvement of these kinases and potentially tackle neuroinflammatory processes, we have focused on three different strategies through the development of multi-target inhibitors, allosteric modulators and covalent inhibitors (Fig. 1). In the first case, we have further optimized a series of several compounds based on a 7-azaindole-3-aminothiazole core that is able to interact with both the kinases through the acceptor-donor template. Particularly, the new library allowed us to investigate how different substitution on the benzyl ring affect the activity. While the ability to simultaneously inhibit multiple kinases involved in neuroinflammation can be useful due to its multifactorial nature, one of the biggest issues dealing with kinases is obtaining selectivity. Covalent inhibition and allosteric modulation are two strategies herein applied to selectively interact with the kinase of interest.

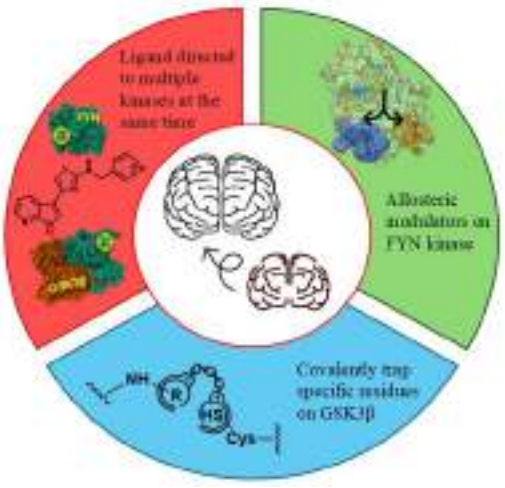

Figure 1. Illustration of the three strategies applied to interact with GSK3β and FYN.

Covalent inhibition can be useful while irreversibly engaging specific residues of the protein that are not shared trough the different kinases. Computational studies on GSK3β demonstrate the presence of a cysteine within the ATP binding site that can be covalently trapped with inhibitory effect. Therefore, based on the same 7-azaindole-3-aminothiazole nucleus, we developed two potential ligands containing electrophilic residues designed to covalently trap the selected cysteine. Regarding the allosteric modulation, we first focused on identifying new potential allosteric pockets in FYN kinase, because they usually involve less conserved residues. Starting from a virtual screening campaign on the two identified allosteric pockets we have obtained 49 molecules which have been evaluated for drug-likeness property and the non-affinity with the ATP site. We are now synthesizing this small library of compounds which will be tested.

REFERENCES

[1] Krahn, A. I.; Wells, C.; Drewry, D. H.; Beitel, L. K.; Durcan, T. M.; Axtman, A. D. Defining the Neural Kinome: Strategies and Opportunities for Small Molecule Drug Discovery to Target Neurodegenerative Diseases. *ACS Chem. Neurosci.* **2020**, *11* (13), 1871–1886. https://doi.org/10.1021/acschemneuro.0c00176.
[2] Marosi M, Arman P, Aceto G, D'Ascenzo M, Laezza F. Glycogen Synthase Kinase 3: Ion Channels, Plasticity, and Diseases. *Int J Mol Sc* **2022**.
[3] Panicker N, Sarkar S, Harischandra DS, Neal M, Kam TI, Jin H, Saminathan H, Langley M, Charli A, Samidurai M, Rokad D, Ghaisas S, Pletnikova O, Dawson VL, Dawson TM, Anantharam V, Kanthasamy AG, Kanthasamy A. Fyn Kinase Regulates Misfolded α-Synuclein Uptake and NLRP3 Inflammasome Activation in Microglia. *J Exp Med.* **2019**. https://doi.org/10.1084/jem.20182191.

P089: ELECTROSPUN PA12 NANOFIBERS FOR POTENTIAL USE AS REINFORCING MEMBRANES IN COMPOSITES

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ABSTRACT

Polymer matrix carbon fiber polymers (CFRPs) offer excellent mechanical properties, often superior to traditional metals, with lower density. Because of these characteristics, their use is increasingly common especially in fields such as aerospace, automotive and sports where there is a need to combine remarkable mechanical properties with limited weights [1]. Laminated CFRPs, which are multilayer materials obtained by overlapping foils consisting of carbon fiber fabrics, have some issues that may limit their more widespread application: delamination and reduced vibration damping (damping) capability.
The scientific community is investigating various methods for countering delamination and increasing damping capacities to improve the quality and safety of laminated composites and extend their service life. The increased durability of the material could make it possible to reduce resource consumption and thus limit the environmental impact of the components.
While the integration of nanofibrous membranes produced from blends consisting of nitrile rubber and polycaprolactone (NBR/PCL) [2,3] is well effective in contrasting delamination, but may lead to loss in other thermomechanical properties. The use of polyamides, especially Nylon 66, is common for reinforcing composites [4].
The purpose of the present experimental work is to produce nanofibrous fabrics made of polyamide 12 for structural modification of epoxy-matrix laminated CFRPs. Initially, the solvent system suitable for solubilizing the polymer and enabling the electrospinning process was identified. Next, ideal process parameters (potential, flow rate, needle-collector distance) were defined to obtain high-quality nanofabrics with single-needle spinning. The obtained membranes were characterized morphologically by SEM (scanning electron microscopy) and thermally by DSC (differential scanning calorimetry) analysis.

REFERENCES

[1] Arussi, E. et al. Composite Materials: A Hidden Opportunity for the Circular Economy
[2] Maccaferri, E., et al. Mater Des 186, 108210 (2020).
[3] Maccaferri E., et al. Mater Des 195, 109049 (2020).
[4] Brugo, T., et al. Compos Struct 154, 172–178 (2016).

P090: STORMING PROJECT - CATALYTIC CONVERSION OF METHANE TO HYDROGEN AND CARBON NANOTUBES: IS MECHANOCHEMISTRY THE GREENER CHOICE? AN LCA STUDY

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ABSTRACT

The rising cost and decreasing supply of fossil fuels have driven the search for clean, alternative energy sources. Hydrogen is a promising clean fuel, but current production methods often generate significant CO_2 emissions [1]. The STORMING project, funded by the European Union's Horizon Europe program, aims to address this challenge by developing a novel catalytic technology that converts methane gas (CH_4) into two valuable products: clean-burning hydrogen fuel (H_2) and carbon nanotubes for batteries. Three universities, within the project consortium, are developing catalysts for this purpose: the University of Bologna using the coprecipitation method, the University of Zaragoza employing the citrate method, and the University of Seville utilizing mechanochemistry.

A life cycle assessment (LCA) [2] is conducted to evaluate the environmental impact of these processes. The LCA methodology involves a comprehensive evaluation of the catalyst's entire life cycle, including both the production impacts and the productivity of the catalysts. This environmental assessment identifies hotspots and conducts an initial screening of the technologies to determine their relative environmental impacts. Additionally, two different pretreatment methods, with and without preliminary catalyst reduction, are compared to assess their respective impacts.

The study's main findings highlight that energy consumption in the mechanochemistry method is a critical issue. Nonetheless, scaling up the process is expected to improve energy efficiency compared to the laboratory-scale version. Additionally, while comparing reductive and non-reductive production methods, reductive catalysts offer minimal efficiency gains but contribute slightly more to environmental impacts.

There are some limitations in this study, as it relies on a laboratory-scale process that may not fully represent the efficiency of large-scale production, and certain data are based on assumptions and estimates. Despite these limitations, the LCA study provides insights into the environmental impact of methane conversion and serves as a guide for advancing more sustainable technology.

REFERENCES

[1] Atilhan, Selma, et al. "Green hydrogen as an alternative fuel for the shipping industry." Current Opinion in Chemical Engineering 31 (2021): 100668.

[2] Curran, Mary Ann. "Life cycle assessment: a review of the methodology and its application to sustainability." Current Opinion in Chemical Engineering 2.3 (2013): 273-277.

P091: ADDRESSING THE DRUG RESISTANCE ISSUE BY TARGETING THE FOLATE CYCLE PROTEINS IN TRYPANOSOMA BRUCEI AND LEISHMANIA MAJOR PARASITES

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ABSTRACT

Human African Trypanosomiasis (HAT), or sleeping sickness, remains a neglected tropical disease despite control programs significantly reducing its prevalence. WHO's 2030 eradication target underscores the need for innovative and collaborative efforts, such as the One Health approach. The disease, caused by *Trypanosoma brucei*, is treated with a limited set of six drugs, including the recently introduced fexinidazole. However, issues of toxicity, resistance, and cost complicate treatment, emphasizing the need for newer, safer, and more effective therapies. Research into targeting folate metabolism enzymes, particularly dihydrofolate reductase (DHFR) and pteridine reductase 1 (PTR1), presents a promising avenue.[1] These enzymes are crucial for parasite proliferation, supporting DNA synthesis and repair. *Trypanosoma* species rely on a bifunctional DHFR-thymidylate synthase, distinct from the human counterpart, making it a viable therapeutic target. Despite nanomolar potency observed in inhibitors against these enzymes, translating this into effective antiparasitic drugs has proven challenging, necessitating further innovation in this area. Addressing folate metabolism in *Trypanosoma* and related parasites like *Leishmania* offers dual potential to combat other parasitic diseases, such as leishmaniasis, where the therapeutic arsenal similarly relies on outdated drugs. Continued research is vital to achieve breakthroughs that can underpin the global eradication efforts for HAT and related diseases. [2] The present work aims to demonstrate the activity of new 1,3,5-triazine derivatives against the dihydrofolate reductase (DHFR) of *Trypanosoma brucei* and *Leishmania major.* The newly synthesized 1,3,5-triazine derivatives were also tested against two additional targets: pteridine reductase 1 of *Trypanosoma brucei* and human DHFR, to evaluate toxicity and preferred species specificity. Furthermore, for both targets, the production and purification protocols were optimized to achieve higher yield. The 1,3,5-triazine derivatives exhibit activity (IC50) in the low micromolar range (1-20μM) against DHFR of *Trypanosoma brucei* and *Leishmania major* while showing activity in the high micromolar range (100-400μM) against pteridine reductase 1 of *Trypanosoma brucei*. Unfortunately,, the compound exhibit activity in the low micromolar range (10-30 μM) also against human DHFR, thus showing a lack of species specificity towards parasitic proteins. In conclusion, we can state that some of these compounds could be promising inhibitors for the treatment of trypanosomiasis when properly developed.

REFERENCES

[1] Francesconi V, et al. Identification of Innovative Folate Inhibitors Leveraging the Amino Dihydrotriazine Motif from Cycloguanil for Their Potential as Anti-*Trypanosoma brucei* Agents. ACS Infect Dis. 2024 Aug 9;10(8):2755-2774. doi: 10.1021/acsinfecdis.4c00113. Epub 2024 Jul 2.
[2] Gibson MW, Dewar S, Ong HB, Sienkiewicz N, Fairlamb AH. Trypanosoma brucei DHFR-TS Revisited: Characterisation of a Bifunctional and Highly Unstable Recombinant Dihydrofolate Reductase-Thymidylate Synthase. PLoS Negl Trop Dis. 2016 May 13;10(5):e0004714. doi: 10.1371/journal.pntd.0004714. PMID: 27175479; PMCID: PMC4866688.

P092: DEVELOPMENT OF A LABEL-FREE IMMUNO-ELECTROCHEMICAL SENSOR FOR CORTISOL DETECTION IN HUMAN SALIVA

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ABSTRACT

Cortisol detection in biofluids is an essential diagnostic tool to monitor stress and health status since cortisol regulates blood pressure, glucose levels, and carbohydrate metabolism[1]. Cortisol levels in serum vary during the day between 100 and 500 nM, while its concentration in saliva is two orders of magnitude lower, between 2,78 and 22,2 nM[2]. Cortisol concentration increases in response to physical conditions such as injury and illness as well as psychological stress[3]. The development of a portable, low cost, accurate and highly sensible sensor for the detection of cortisol in human saliva provides advantages like fast measurements and non-invasive sample collection[1]. In order to realize a point-of-care (POC) compatible detection system based on an immuno-electrochemical sensor on gold surfaces, bulk gold electrodes were functionalized with monoclonal mouse anti-cortisol antibodies via linking with 3,3′-Dithiodipropionic acid di(N-hydroxysuccinimide ester) (DTSP). Electrochemical impedance spectra are represented in the form of Nyquist plots to highlight the modification in charge transfer resistance (R_{ct}) at the sensor-solution interface during each step of functionalization (Figure igure 1): (1) bare gold electrode (R_{ct} 6500 Ω), (2) DTSP layer (R_{ct} 9000 Ω), (3) anti-cortisol antibody layer (R_{ct} 12500 Ω) and (4) cortisol binded to the immunosensor (R_{ct} for 10 nM cortisol 22500 Ω). The significant increase in R_{ct} caused by 10 nM cortisol suggests that this immunosensing approach could be effective for salivary cortisol determination. Cortisol quantification is realized by recording calibration curves within the biologically relevant ranges. Future perspectives for this project include the miniaturization of the system and establishing large-scale production of disposable POC sensors by employing ink-jet printed gold electrodes.

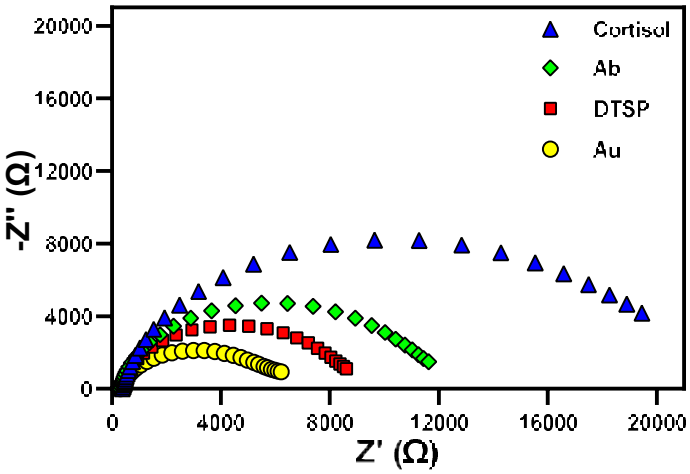

Figure 1: Nyquist plots of (○) bare gold electrode, (□) functionalization with DTSP, (◇) functionalization with anti-cortisol and (△) binding with cortisol from a 10 nM cortisol solution.

REFERENCES

[1] Stevens, R. C., Soelberg, S. D., Near, S. & Furlong, C. E. Detection of cortisol in saliva with a flow-filtered, portable surface plasmon resonance biosensor system. Anal Chem 80, 6747–6751 (2008).
[2] Arya, S. K., Chornokur, G., Venugopal, M. & Bhansali, S. Antibody functionalized interdigitated μ-electrode (IDμE) based impedimetric cortisol biosensor. Analyst 135, 1941–1946 (2010).
[3] Kämäräinen, S. et al. Disposable electrochemical immunosensor for cortisol determination in human saliva. Talanta 188, 50–57 (2018).

P094: ASSESSMENT OF DRUG-BINDING LEVELS TO HUMAN SERUM ALBUMIN BY SURFACE PLASMON RESONANCE APPROACH

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ABSTRACT

Human Serum Albumin (HSA) is one of the most abundant plasma proteins (35-50 g/L)[1]. HSA performs several critical functions, such as maintaining oncotic pressure, regulating the bloodstream pH, and transporting insoluble and hydrophobic endogenous and exogenous ligands, including drugs. Binding to HSA modulates drug bioavailability in human blood[2]. Thus, serum albumin–drug binding is an important pre-ADME parameter since bound/unbound fraction can strongly influence drug pharmacokinetics and pharmacodynamics.
Within med chem collaboration projects, we focused on the investigation of the affinity constants and estimation of free drug of a series of small molecule compounds toward HSA. To reach this goal, a Surface Plasmon Resonance (SPR)-based approach was selected. SPR allows to monitor association and dissociation events within a biorecognition process in real-time without the need to label the target protein.
To perform such studies, a sensor chip functionalized with the target protein, namely HSA, should be prepared and validated. Following previous studies, HSA immobilization was accomplished by covalent immobilization on a gold sensor chip surface functionalized with carboxymethylated dextran chains (CM5)[2] exploiting a well-established an amine coupling reaction. Before use, the functionalized sensor chip was validated to confirm binding properties were not altered by the immobilization process. This was achieved by assessing HSA affinity for known binders. The validated sensing surface was then applied to determine the affinity constants (K_D) of selected compounds, which were selected based on their promising activity and safety profiles. The final aim was to use in vitro data to estimate drug bound/unbound fraction to complement in vivo pharmacokinetic studies. Hence, the drug bound fraction (%) Considering an HSA plasma concentration of 680 μM, the percentage of protein binding was also derived from K_D values using the equation proposed by Liu et al.[4].

REFERENCES

[1] Petitpas I, Bhattacharya AA, Twine S, East M, Curry S. Crystal structure analysis of warfarin binding to human serum albumin. Anatomy of drug site I. *Journal of Biological Chemistry*. 2021, 276, 25, 22804-9. doi:10.1074/jbc.M100575200
[2] Yamasaki K, Chuang V.T.G, Maruyama T, Otagiri M. Albumin–drug interaction and its clinical implication. *Biochimica et Biophysica Acta (BBA) - General Subjects.* 2013, 1830, 12, 5435-5443. doi.org/10.1016/j.bbagen.2013.05.005
[3] Fabini E, Tramarin A, Bartolini M. Combination of human acetylcholinesterase and serum albumin sensing surfaces as highly informative analytical tool for inhibitor screening. *J Pharm Biomed Anal*. 2018, 5, 155, 177-184. . doi:10.1016/j.jpba.2018.03.060
[4] Liu, X.; Song, D.; Zhang, Q.; Tian, Y.; Liu, Z.; Zhang, H. Characterization of Drug-Binding Levels to Serum Albumin Using a Wavelength Modulation Surface Plasmon Resonance Sensor. *Sens Actuators B Chem* 2006, 117, 1, 188–195. https://doi.org/10.1016/J.SNB.2005.11.023

P095: BIO-NANO INTERACTIONS OF FUNCTIONAL DNA ORIGAMI TARGETING CELL RECEPTORS

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ABSTRACT

The DNA origami technique streamlines the independent assembly of customizable DNA structures, enabling precise patterning at the nanoscale of a variety of conjugated biomolecules. With their inherent compatibility with biological systems and the ability to control shape, size, and ligand arrangement, DNA-based nanostructures hold great promise for applications in nanomedicine1,2. Despite demonstrations of effective binding in various scenarios, the underlying biophysical dynamics governing membrane binding remain largely unexplored. In this study, we explore the binding dynamics of two rod-shaped DNA origami nanoconjugates: one decorated with anti-EGFR (Epidermal Growth Factor Receptor) antibodies and the other with anti-EGFR aptamers. Through single-particle tracking (SMT) microscopy, we monitor the trajectories of ligand-modified DNA origami in both free solution and bound states on the cell membrane, enabling the calculation of their diffusion coefficient (D). We show that we can quantify the fraction of DNA origami specifically bound to the targeted receptor, distinguishing them from nonspecific bindings. Furthermore, SMT aids in determining the first-order rate constant for complex dissociation (Koff), a critical parameter revealing the average duration of the interaction between the DNA origami and the membrane receptors. The ability to finely adjust Koff values can be crucial for modulating potential therapeutic and stimulation effects3. Our DNA origami nanoconjugates demonstrate specific binding with a Koff profile potentially favoring preferential binding to cancer cells, opening new avenues in selective cell targeting for biomedical applications.

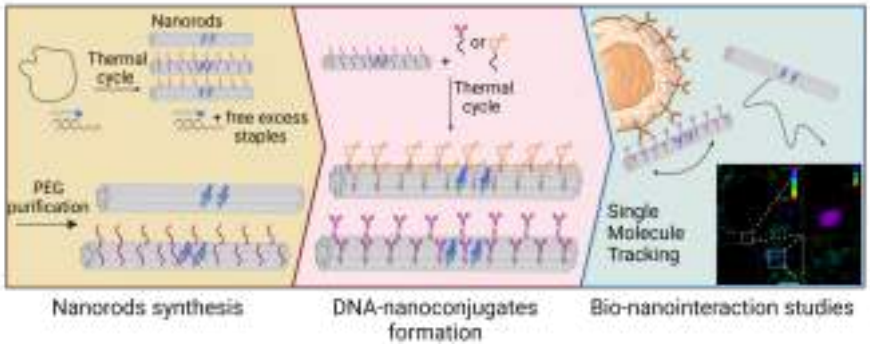

Figure 1. Schematic rendering of the workflow

REFERENCES

[1] Wagenbauer, K. F. et al. Nature Nanotechnology. 2023, 18, 1319–1326
[2] Zhang, P. et al. Nature Communications. 2020, 11:3114
[3] Corzo, J. Biochemistry and Molecular Biology Education. 2006, 34:413–416

P096: SYNTHESIS OF ARTIFICIAL METALLOPROTEINS BASED ON THE SPYCATCHER-SPYTAG SYSTEM FOR HYDROGEN PRODUCTION

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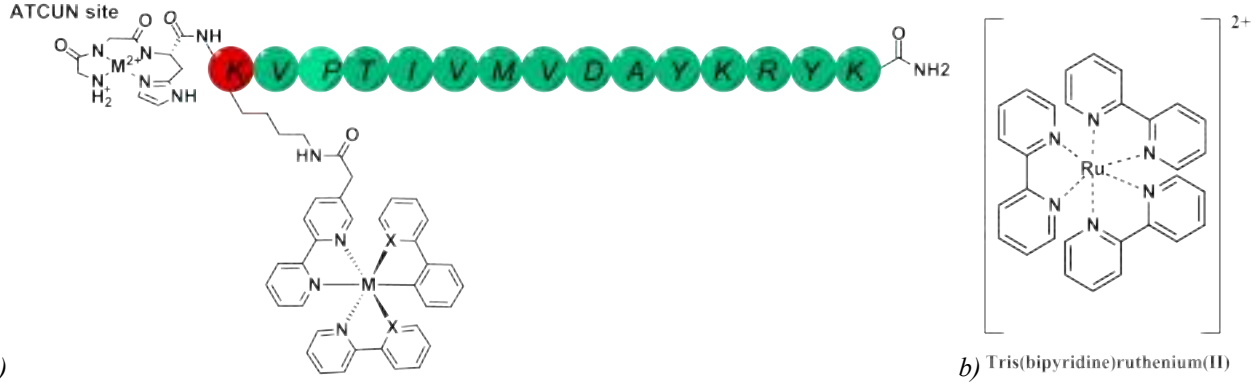
ABSTRACT

The SpyCatcher-SpyTag system is a versatile system that allows metal centres to be introduced into protein systems by functionalizing a peptide (SpyTag) that spontaneously reacts with a complementary protein (SpyCatcher). The bond formed between the two components is isopeptide, between the side chains of a lysine (Lys) on SpyCatcher and the carboxyl of an aspartate side chain (Asp)on SpyTag. The two components react spontaneously at room temperature and form a covalent complex [1]. It has been observed that tris(bipyridyl)ruthenium(II) chloride $[Ru(Bpy)_3]Cl_2$ is a complex with special photochemical characteristics. [2] The absorption of light by $[Ru(Bpy)_3]^{2+}$ leads to the formation of a long-lived excited state. In its excited state, this complex possesses reducing characteristics, with an extremely low oxidation potential capable of reducing H^+ to ½ H_2 [2]. Although this reduction is not kinetically favoured, the ruthenium complex can reduce a redox centre which, in turn, is catalytically active for this hydrogen-producing reaction. Therefore, the $[Ru(Bpy)_3]^{2+}$ group will be grafted to the SpyTag using a heteroleptic ruthenium complex, in which there is a carboxylate group on one of the ligands. The project proposal concerns the synthesis of SpyTag peptides containing a catalytic centre (e.g. an ATCUN (Amino Terminal Copper and Nickel Motif) site coordinating Co(III) ion) and a photocatalytic group (e.g. Ru(II)). The resulting photoactive SpyTag that can be bound to a SpyCatcher, giving a new artificial metalloenzyme.



a) *b)*

Figure 5: *a)* Spy Tag containing the ATCUN site for binding to the catalytic group and a modified lysine for binding to the photocatalytic group; *b)* Photocatalytic group: tris(bipyridyl)ruthenium(II)

Project "Artificial enzymes for the photocatalytic production of hydrogen in photosynthetic bacteria" National Recovery and Resilience Plan (NRRP), M2 C2 Inv. 3.5 funded by the European Union – NextGenerationEU. Project RSH2A_000009, C.D. 445 29/12/2022 Italian Ministry of Environment and Energy Security. "Bando di Ateneo per la Ricerca 2022" – A Way Towards Artificial Metalloenzymes - University of Parma

REFERENCES

[1] D. Hatlem, T. Trunk, D. Linke, and J. C. Leo, *Int J Mol Sci*, vol. 20, no. 9, May 2019, doi: 10.3390/ijms20092129.
[2] M. Hara, C. C. Waraksa, J. T. Lean, B. A. Lewis, and T. E. Mallouk, *Journal of Physical Chemistry A*, vol. 104, no. 22, pp. 5275–5280, Jun. 2000, doi: 10.1021/jp000321x.

P097: 2,6-DIIMINOPYRIDINE-BASED ORGANOMETALLIC PRE-CATALYSTS: SYNTHETIC STUDIES AND CATALYTIC APPLICATIONS

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ABSTRACT

A key issue in modern catalysis is the reliance on precious metals in homogeneous processes. While catalysts based on rare metals are critical for producing fine chemicals and various commodities, hurdles such as volatile market prices, limited supply, toxicity, and environmental impact have driven researchers to investigate first-row transition metals as sustainable alternatives.[1] In particular, first-row transition metal complexes bearing 2,6-diiminopyridines (^{R_1,R_2}PDI) and alkyl ligands (X in Fig. 1) have demonstrated to be highly effective pre-catalysts in olefin chemistry.[2] However, their scalable production and storage are challenging due to their exceedingly high air-sensitivity and thermal instability.

We herein describe the *in-situ* preparation of [(^{R_1,R_2}PDI)MX_2] complexes starting from ^{R_1,R_2}PDI ligands and a relatively stable organometallic precursor [(L)MX_2], with the possible addition of an ancillary inorganic lithium salt to favour the displacement of the labile ligand L. The ligand exchange reaction occurs in an organic solution with promising conversions and minimal formation of undesired dealkylation products, as confirmed by ^{1}H NMR spectroscopy.

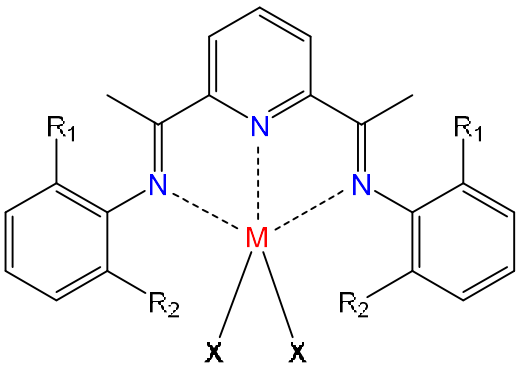

Figure 1. Structure of ^{R_1,R_2}PDI metal complexes

Moreover, conversion tends to increase with decreasing steric hindrance of the aryl groups, as determined by the R_1 and R_2 substituents.

This *in-situ* assembly protocol was applied in a benchmark hydrosilylation reaction between 1-octene and triethoxysilane. Conversion and selectivity, assessed *via* ^{1}H NMR spectroscopy, ranged from good to excellent and were comparable with those obtained using analogous pre-catalysts prepared *ex-situ*.[2]

Therefore, our technique affords a viable strategy for the large-scale production of ready-to-use [(^{R_1,R_2}PDI)MX_2] pre-catalysts in organic solvents and supports their application in industrially relevant organic reactions.

REFERENCES

[1] Supanchaiyamat, N.; Hunt, A. J.; *ChemSusChem* **2019**, *12*, 397–403

[2] Obligacion, J. V.; Chirik, P. J; *Nat. Rev. Chem*. **2018**, *2*, 15–34

P098: CARBOXYLIC *vs* AMIDE DONOR GROUPS FOR Pb^{2+} COMPLEXATION IN NUCLEAR MEDICINE

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ABSTRACT

Lead-212 ($t_{1/2}$ = 10.6 h, E_{β^-} = 100 keV, I_{β^-} = 100%, in vivo α-particle generator) and lead-203 ($t_{1/2}$ = 51.9 h, E_γ = 279.1 keV, I_γ = 81%, SPECT) offer the rare opportunity to have a theranostic pair comprising an alpha-emitter with moderate half-life, which has driven increased interest in nuclear medicine applications [1]. According to the Pearsons' Hard Soft Acid Base classification, Pb(II) is a borderline soft metal ion, and it preferentially binds to soft donor atoms, such as nitrogen, sulphur and oxygen. To date, the $[^{203/212}Pb]Pb^{2+}$ complexation has been performed with the macrocyclic 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) and its amide derivative TCMC (or DOTAM)[2]. While DOTA has been widely used, it suffers of acidic dissociation, resulting in the release of the metal; moreover, it does not effectively retain the daughter radionuclide ^{212}Bi, which tends to accumulate in the kidneys. TCMC, on the other hand, has a higher kinetic inertness, but the retention of the daughter radionuclide is still an issue [3]. Recent studies have focused on developing new systems incorporating amide and carboxylic donor atoms, highlighting the importance of matching the donor atoms with the chelator scaffold [1,4].

Herein, we have designed new ligands incorporating "rigid" *trans*-diamminocyclohexane (DACH) backbone, which can improve the kinetic inertness and the thermodynamic stability through a pre-organized structure [Fig.1]. H_2bpcd is a ligand already known in literature [5], but to our knowledge, it was never used for Pb^{2+} complexation. Pb^{2+} complexation was studied using ^{1}H-NMR spectroscopy. Complex formation kinetics was investigated in different buffered conditions (pH 2, 4.4, 7.4). Immediately after metal addition, the changes in the ^{1}H-NMR spectra pointed out the complex formation. This was further confirmed by HR-MS(ESI). No additional changes were observed afterwards, suggesting a rapid kinetic in a wide pH range. For NH_2bpcd, multiple isomers were observed, with one being predominant, while H_2bpcd exhibited a predominant one. Ongoing studies are investigating the thermodynamic stability of these complexes, and future experiments will aim to elucidate the complex structures, giving further insight on the coordination environment.

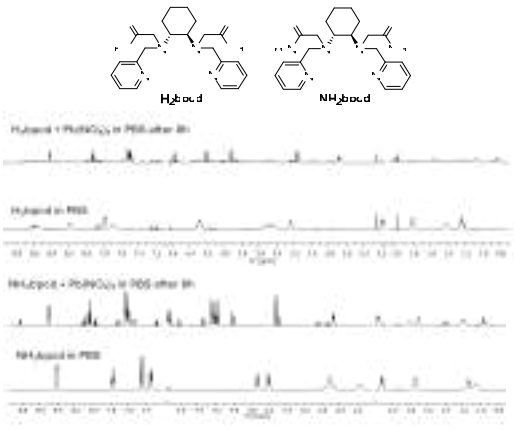

Figure 1. Structures of H_2bpcd and NH_2bpcd (top) and kinetic experiments with $Pb(NO_3)_2$ in PBS *via* ^{1}H-NMR (bottom).

REFERENCES

[1] A. Ingham *et al.*, Getting a lead on Pb^{2+}-amide chelators for $^{203/212}Pb$ radiopharmaceuticals, *Dalton Trans.* 2021, 50, 11579–11595.
[2] E. W. Price and C. Orvig, Matching Chelators to radiometals for radiopharmaceuticals, Chem. Soc. Rev., 2014, 43, 260.
[3] M. Tosato *et al.*, Tuning the Softness of the Pendant Arms and the Polyazamacrocyclic Backbone to Chelate the $^{203}Pb/^{212}Pb$ Theranostic Pair, *Inorg. Chem*. 2024, 63, 1745−1758.
[4] A. Ingham *et al.*, H_2ampa - Versatile Chelator for $[^{203}Pb]Pb^{2+}$, $[^{213}Bi]Bi^{3+}$, and $[^{225}Ac]Ac^{3+}$, *Inorg. Chem*. 2022, 61, 9119−9137.
[5] J. Florián *et al.*, Metal Ion Complexes of N,N′-Bis(2-Pyridylmethyl)-trans-1,2-Diaminocyclohexane-N,N′-Diacetic Acid, H2bpcd: Cis/Trans Isomerization Equilibria, *Inorg Chem*. 2015, 21, 10361–10370.

P099: MICROFLUIDIC LNPS OPTIMIZATION TO IMPROVE PDNA LOADING AND SAFETY PROFILE

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ABSTRACT

Several nanomedicine (NMed) systems were demonstrated to be able to protect, target, and transfect genes *in vitro*. Although the interest in gene therapy is growing, efficient and scalable methods for industrial production don't exist. To overcome this problem, microfluidic (MF) technology, which became famous thanks to the production of vaccines for COVID-19, is a promising option [1-2]. This technique employs automated pump systems to drive solvents containing the drugs and materials necessary to form the NMed through a MF chip. The use of such a system allows for the creation of NMed formulations with enhanced output, greater reproducibility, and the potential for full automation. Furthermore, this method offers the possibility of scaling up production in compliance with Good Manufacturing Practice (GMP) standards [3-4]. Crucial parameters to optimise are total flow rate (TFR), flow rate ratio (FRR), total volume, concentrations of the materials and storage and stability conditions [5-6]. Moreover, it was fundamental to consider these aspects for each drug and NMed combination individually to achieve satisfying results both *in vitro* and *in vivo*. This work focused on the optimisation of the MF technique to produce plasmid DNA (pDNA)-loaded lipid nanoparticles (LNPs) to create methodology that is translatable from the classic techniques. Phospholipids and cholesterol were employed to create lipid LNPs using a MF chip. A cationic and neutral formulation were compared to determine whether the cationic charge was essential during the formulation process. The former was obtained using DPPC, cholesterol and DOTAP, the latter was produced with DPPC and cholesterol. Plasmid DNA was introduced to pre-formed liposomes, similar to traditional benchtop techniques, or directly during the formulation process as a solution in the aqueous phase. Both approaches were evaluated for size, uniformity, encapsulation efficiency, stability, and underwent *in vitro* uptake and localization studies. Results show that cationic LNPs were able to carry 10 times more DNA than the traditional method, while neutral LNPs, which also loaded and protected the DNA, exhibited lower toxicity and effective DNA protection. This represents a significant advancement in reducing both the required doses and the toxicity of LNP-based gene therapies.

REFERENCES

[1] Maeki M, Okada Y, Uno S, et al. Appl Mater Today. 2023;31:101754. doi:10.1016/j.apmt.2023.101754
[2] Huang Y, Liu C, Feng Q, Sun J. Nanoscale Horiz. 2023;8:1610–1627. doi:10.1039/D3NH00217A
[3] Ejeta F. DDDT. 2021;15:3881–3891. doi:10.2147/DDDT. S324580
[4] Jaradat E, Weaver E, Meziane A, Lamprou DA. Nanomaterials. 2021;11:3440. doi:10.3390/nano11123440
[5] Prakash G, Shokr A, Willemen N, et al. Adv Drug Delivery Rev. 2022;184:114197. doi:10.1016/j.addr.2022.114197
[6] Gimondi S, Ferreira H, Reis RL, Neves NM. ACS Nano. 2023;17:14205–14228. doi:10.1021/acsnano.3c01117

P100: MS PROTEOMICS AND BIOCHEMICAL CHARACTERIZATION OF THYMIDYLATE SYNTHASE DIMER DESTABILIZER E7 TO HALT COLORECTAL CARCINOMA

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ABSTRACT

Colorectal cancer (CRC) is a leading cause of cancer-related deaths worldwide, with treatment efficacy often limited by resistance to standard chemotherapy. 5-Fluorouracil (**5-FU**), a primary chemotherapeutic agent for CRC treatment, acts by stabilizing thymidylate synthase (TS) in its dimeric form, inadvertently promoting TS accumulation and reducing its efficacy due to resistance mechanisms linked to TS overexpression and stabilization. To address the drug resistance challenge, the Drug Discovery and Biotechnology Lab (UniMORE) has developed innovative TS dimer destabilisers (DDIs) that bind to an allosteric TS site at the monomer interface [1]. DDIs promote TS dimer dissociation into monomer, which is catalytically inactive, leading to TS degradation via the proteasome and minimizing drug resistance, in contrast to **5-FU**'s dimer-stabilizing mechanism [1]. **E7** demonstrates a comparable *in vitro* and *in vivo* (ectopic mice models of pancreatic cancer) comparable to **5-FU**, but less risk to develop drug resistance [2].

In the present study, we aim to characterize the molecular mechanism of action of **E7** when administered to CRC cells, and the main metabolic pathways activated with respect to **5-FU** that drive cancer cell deaths. Through time-lapse MS-based proteomic analysis of HCT-116 cells treated with **5-FU** and **E7** after 6 and 12h, we demonstrate that **E7** activates DNA damage response pathways, inhibits cell cycle progression at the G2/M checkpoint, and triggers apoptosis, effectively targeting cellular pathways that **5-FU** does not. Functional bioinformatics and network analysis further reveal that **E7** selectively modulates proteins associated with DNA repair, nucleotide metabolism, and proteasome activity, suggesting a distinct and targeted mechanism of action with respect to 'traditional' false nucleosides. This mechanistic insight will be furtherly validated using molecular biology techniques, including cell cycle analysis and the measurement of DNA damage biomarkers, and in a translational approach on patient-derived 3D CRC organoids, on which preliminary results suggest that their potency is comparable to 5-FU.

This study establishes **E7** as a promising therapeutic candidate with a novel mechanism of TS inhibition and finally explains its molecular mechanism of action, that makes it different from 5-FU and antifolates. These findings provide a strong foundation for future development of novel anticancer agents as a new class of drug aimed at mitigating drug resistance in several types of solid carcinomas.

REFERENCES

[1] Costantino L, *et al*. Destabilizers of the thymidylate synthase homodimer accelerate its proteasomal degradation and inhibit cancer growth. Elife. 2022 Dec 7;11:E73862. doi: 10.7554/eLife.73862.

[2] Marverti G. *et al*. Enhanced anticancer effect of thymidylate synthase dimer disrupters by promoting intracellular accumulation. Front. Pharmacol., 11 November 2024. Volume 15 - 2024 | https://doi.org/10.3389/fphar.2024.1477318

P101: LOCALLY-WEIGHTED-ROBOOST-PLS: A REGRESSION MODEL FOR SIMULTANEOUS HANDLING OF NON-LINEARITIES AND OUTLIERS

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ABSTRACT

Partial Least Squares (PLS) regression is a common approach in chemometrics for modelling relationships between independent and dependent variables. However, traditional PLS models are limited when faced with non-linear relationships or outliers. To address these challenges, methods such as Locally Weighted PLS (LW-PLS) and RoBoost-PLS have been developed. LW-PLS deals with non-linearities by creating, for each new incoming sample, a local calibration models based on the nearest neighbours, while RoBoost-PLS reduces the influence of outliers by down-weighting their importance in the PLS training process. Unfortunately, none of these techniques can address both issues simultaneously when they co-occur in the data (see Figure 1a-b-c).

In this work, a novel hybrid method called Locally-Weighted-RoBoost-PLS (LW-RoBoost-PLS) is proposed, which couples the principles of LW-PLS and RoBoost-PLS to efficiently deal with these particular situations. Similar to LW-PLS, LW-RoBoost-PLS constructs local regression models for each new sample at hand, but the coefficients of these regression models are calculated by the RoBoost-PLS algorithmic procedure rather than by standard PLS. This allows the impact and influence of outliers to be reduced at a local level, while still providing a meaningful description of possible non-linear relationships between predictors and responses.

The performance of LW-RoBoost-PLS will be evaluated here and compared with that of LW-PLS and RoBoost-PLS in various simulated case studies [3] and in a real industrial scenario. The results of this study will show that LW-RoBoost-PLS can significantly reduce the prediction bias typically caused by nonlinearities, while at the same time reducing the prediction instability typically caused by anomalous data (see Figure 1d).

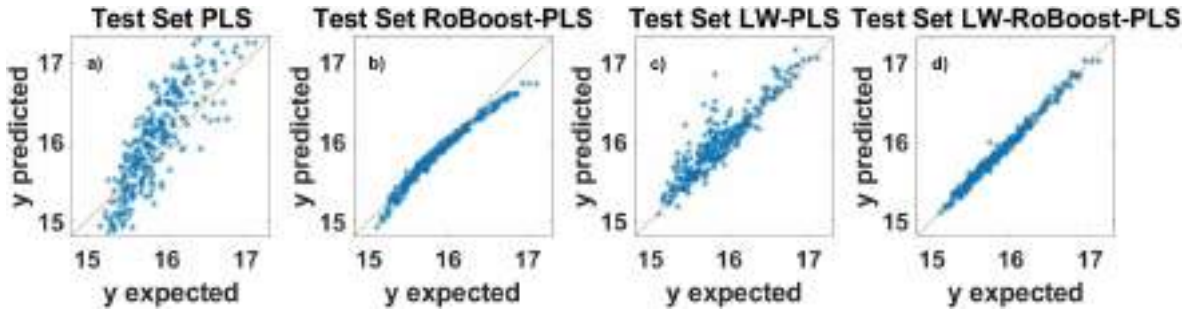

Figure 6 predicted y-values versus measured y-values plots resulting from the application of the optimal **a)** PLS **b)** RoBoost-PLS, **c)** LW-PLS-R and **d)** LW-RoBoost-PLS models

REFERENCES

[1] M. Metz, M. Lesnoff, J.-M. Roger, J. Chemom. 34 (2020) e3209.
[2] M. Metz, F. Abdelghafour, J.-M. Roger, M. Lesnoff, Anal. Chim. Acta. 222 (2021) 104498.
[3] M. Metz, A. Biancolillo, M. Lesnoff, J.-M. Roger, Chemom. Intell. Lab. Syst. 200 (2020) 103979.

P102: EXPLORING THE POTENTIAL OF CHIRAL MONOAMIDINE CATALYSYS IN APIs PRODUCTION

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ABSTRACT

In this study, we present the synthesis and application of chiral monoamidine organocatalysts in the stereoselective synthesis of APIs (Active Pharmaceutical Ingredients) with potent biological activity. In this regard, inspired by the pioneering work of Johnston's group,[1,2] a new class of supported chiral monoamidine organocatalysts (Benz-MAM) has been developed and first tested in the stereoselective aza-Henry reaction under heterogeneous phase, leading to the pivotal β-amino nitroalkane precursors of the anti-cancer agents Nutlins (with Nutlin-3a as the most active drug). Different synthetic strategies for immobilization on various supports have been investigated, followed by the evaluation of catalytic activity under heterogeneous phase. The monolithic macroporous PS-BenzMAM organocatalyst showed the best activity among the tested catalysts in terms of yield, reaction time, and stereoselectivity, achieving high yield (up to 99%), *ee* up to 99%, and dr up to 99:1 in the synthesis of a short library of Nutlin-3a analogues. The catalyst's recyclability was also evaluated, through simple filtration, yielding a satisfactory 90% *ee* after 5 cycles, showing only a moderate decrease in conversion efficiency (ca. 3% after each cycle). Next, we explored the applicability of this class of organocatalysts for direct access to chiral decorated oxindole, a pharmacologically privileged scaffold with biological properties relevant to medicinal chemistry[3] Many synthetic protocols have been reported to produce this class of molecules using both asymmetric metal [4] and organocatalysis.[5] In this context, Benz-MAM organocatalysts had not been explored before. Considering the satisfactory results achieved in the synthesis of Nutlin precursors, chiral Benz-MAM have been employed in an highly diastereo- and enantioselective nitro-Mannich reaction of isatin-derived ketimines with α-aryl nitromethane, leading to 2-oxindoles with a quaternary stereocenter in 3-position, an important chiral structural motif for bioactive natural products and drug candidates. The process was first investigated in homogeneous phase, synthetizing a collection of 3-substituted 3-amino-2-oxindoles with excellent results in terms of yield (up to 99%) and stereoselectivity (*ee* up to 97%, dr up to 97:3). Finally, preliminary studies on the use of chiral supported PS-Benz-MAM in heterogeneous phase have been carried out.

Figure 1: Exploring the potential of chiral monoamidine catalysis

[1] T. A. Davis; J. N. Johnston; *Chem. Sci*., **2011**, 2, 1076; [2] B. A. Vara; A. Mayasundari; J. C. Tellis; M. W. Danneman; V. Arredondo; T. A. Davis; J. Min; K. Finch; R. K. Guy; J. N. Johnston; *J. Org. Chem*.; **2014**, 79, 6913−6938; [3] Y. M. Khetmalis; M. Shivani; S. Murugesan; K. V. G. C. Sekhar; *Biomedicine & Pharmacotherapy;* **2021**; 141; 111842; [4] J. Ma; X. Ding; Y. Hu; Y. Huang; L. Gong; E. Meggers; *Nature Comm*.; **2014**, 5, 4531; [5] Y. Hu; Z. Zhou; L. Gong; E. Meggers; *Org. Chem. Front.;* **2015**, 2, 968–972.

P103: SYNTHESIS AND CHARACTERIZATION OF TWO-STATIONS ONE-GATE CALIX[6]ARENE BASED ORIENTED ROTAXANE ISOMERS

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ABSTRACT

The design, construction and operation of devices and machines at the molecular scale using the bottom-up approach captivates a lot of interest in nanoscience. Particularly intriguing are species composed of interlocked molecular components, making them ideal candidates for these aims.[1] For example, [n]pseudorotaxanes, [n]rotaxanes and [n]catenanes are versatile prototypes for constructing molecular machines because they can be engineered to execute a diverse range of functions, including mechanical-like movements in response to chemical, photochemical, or electrochemical stimuli.[2]
In this context, our research group is engaged in developing prototypes of molecular machines using macrocyclic derivatives based on calix[6]arenes. These derivatives exhibit high affinity in non-polar solvents towards redox-active N,N'-dialkylviologen salts.[2]
The aim of this work was the design, synthesis, and characterization of two orientational isomers of [2]rotaxanes based on a tris-N-phenylureido calix[6]arene derivative (**W**, **Figure 1**),[3] intended for use as prototypes of molecular machines. The preparation of these mechanically interlocked compounds relied on a templated approach, involving the formation of two oriented pseudorotaxanic isomers where the axial component is a viologen salt featuring hydroxyl groups at both ends, enabling subsequent locking through a protection reaction. The design of the axial precursor (**A**, **Figure 1**) was conceived to allow the realization of the [2]rotaxane (**R$_{up}$** and **R$_{down}$**, **Figure 1**). This precursor features two stations separated by a gate. The stations are functionalities that exhibit a pronounced affinity for the aromatic cavity of W. The gate consists of an isomerizable group designed to either permit or hinder the shuttle movement of **W** between the two stations of **A**.

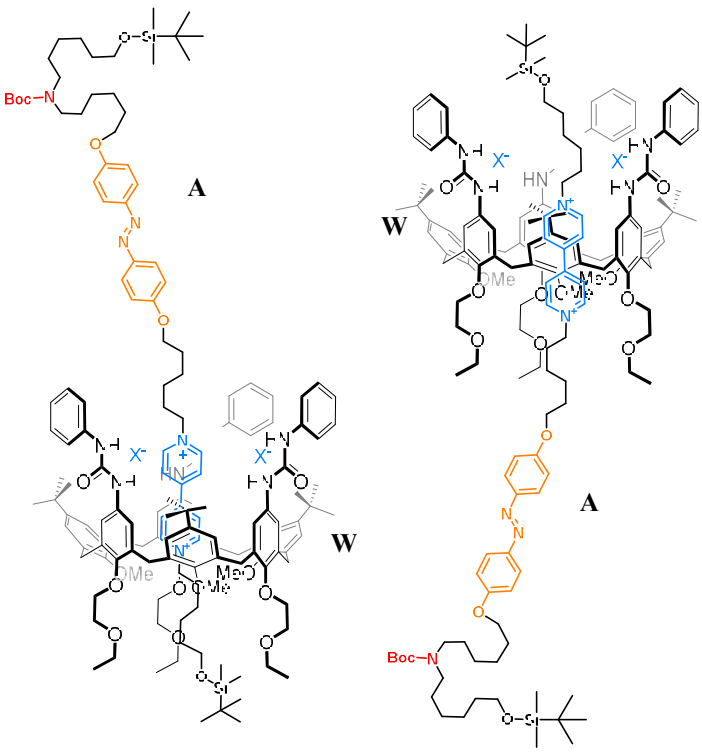

Figure 7. Schematic representation of the oriented [2]rotaxane R_{up} (right) and R_{down} (left)

REFERENCES

[1] V. Balzani, A. Credi, M. Venturi; NanoToday, 2007, 2(2), 18–25.
[2] A. Credi, S. Dumas, S. Silvi, M. Venturi, A. Arduini, A. Pochini, A. Secchi; J. Org. Chem., 2004, 69, 5881–5887.
[3] G. Cera, A. Arduini, A. Secchi, A. Credi, S. Silvi, The Chemical Record 2021, 21, 1161–1181.

P104: CYTOTOXIC NI(II) THIOSEMICARBAZONE COMPLEXES: XRD AND BIOMOLECULAR INTERACTIONS

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Bando di Ateneo per la Ricerca 2022 -*A Way Towards Artificial Metalloenzymes*- University of Parma

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ABSTRACT

In this work we propose Ni(II) coordination compounds involving four thiosemicarbazone ligands. On one hand this category of chelators is well-known for its biological applications and for its versatility to bind various metals[1–2]; on the other hand, similar Ni(II) complexes with thiosemicarbazones revealed to be cytotoxic towards cancer cells[3]. We firstly characterized the coordination compounds via NMR, IR, ESI-MS, UV, EA and XRD to understand their structure and chemical properties. These analyses showed that *E* thiosemicarbazones isomerize to *Z* on the metal ion in order to favour the formation of 2:1 square planar complexes, employing a *trans* coordination configuration around Ni(II).

These complexes were tested against a wide spectrum of cancer cells line, revealing that two complexes (i. e. **Ni(L2)$_2$** and **Ni(L4)$_2$**) display strong efficacy.

We therefore hypothesized two main modes of action: reactive oxygen species (ROS) related mechanism and direct interaction with DNA. ROS scavenging properties were tested spectroscopically mixing the target complexes with DPPH, superoxide, hydroxyl radical and hydrogen peroxide, showing moderate activity. On the other hand, circular dichroism showed a probable interaction at high concentration with DNA; in addition, fluorescence ethidium bromide assay showed that all four complexes display high binding constants towards DNA at low concentration. We therefore support that it is more probable an interactive mode of action with DNA. Albumin is a highly concentrated sequestrant species in human blood, so we tested whether it represented a menace to our compounds diffusion in human circular system. We employed circular dichroism and IR for a qualitative assay, and fluorescence quench titrations to obtain K_b values. These assays resulted in a moderate affinity: considering that albumin is present as well in the growth medium of the cancer cells during cytotoxicity assays, it seems that albumin does not chelate strongly enough to hinder cytotoxicity. Plausibly, it works more as a delivery system.

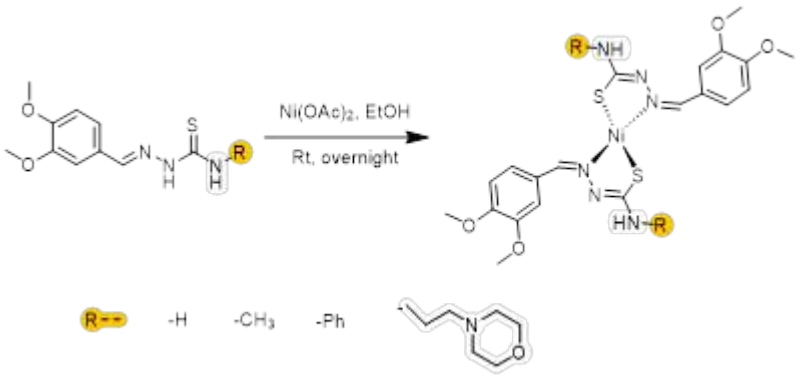

Figure 1: Synthesis of the complexes.

REFERENCES

[1] G. Pelosi, Open Crystallogr. J. 2010, 3, 16–28.

[2] B. Kumar, J. Devi, A. Dubey, A. Tufail, S. Sharma, Inorg. Chem. Commun. 2024, 159, 111674.

[3] J. Garcìa-Tojal, A. Garcìa-Orad, A. Alvarez Dìaz, Juan Luis Serra, M. K. Urtiaga, M. I. Arriortua, T. Rojo, J. Inorg. Biochem. 2021, 271-278.

P105: THERMODYNAMIC UNDERSTANDING OF CNT FORMATION: CAN A BYPRODUCT BE MORE VALUABLE THAN THE MAIN PRODUCT?

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ABSTRACT

Carbon nanotubes (CNTs) are allotropic structures of carbon that, since they were characterized in 1991 by Iijima [1], have demonstrated significant potential in numerous scientific fields such as chemistry, physics and electronics and therefore considered high added-value products. A noteworthy method for their production is catalytic methane decomposition (CMD), a promising reaction to produce turquoise hydrogen which uses hydrocarbons as feedstock for hydrogen source (kind of blue hydrogen) and is CO_2-free (kind of green hydrogen) [2]. This process involves the use of catalytic metal nanoparticles e.g., Ni, Co, Fe supported on inert substrates such as SiO_2 or Al_2O_3. Depending on the operational conditions, the reaction can yield either carbonaceous deposits that can permanently inhibit catalytic activity (encapsulation) [3] or even detach the metal nanoparticle from the substrate (tip-growth) [4]. Alternatively, favorable conditions can lead to high added-value through the base-growth mechanism [4], such as CNTs. The latter play a crucial role in reducing the effective cost of H_2 production and meeting targets set by regulatory bodies, such as the U.S. Department of Energy's goal of $ 2/kg by 2026 and $ 1/kg by 2031 [5]. Controlling carbonaceous byproduct during CMD is essential for extending catalyst lifespan and producing high added-value compounds. This study proposes a thermodynamic model inspired to the 'sharp interface model' largely used in the interface physics of fluids, which separates bulk energy contributions from interface-specific effects, and includes an equation to calculate the driving force governing the competition between nanotube growth and cap expansions. Being the atomistic details of the formation and growth of carbon nanotubes experimentally inaccessible, *ab-initio* (density functional theory) simulations were performed to compute the energetic terms of the thermodynamic model. Large Ni and Co catalytic nanoparticles were modeled using slabs, exposing their most stable facets. First, the energetic adsorption of various carbon structures, denoted as patches and caps, on metal catalysts surfaces was investigated to identify the thermodynamically favored configurations. Despite the greater curvature and ring defects of the caps, they were found to be more stable than the patches. Subsequently, the driving force for cap growth over nanotube formation was analyzed, with results showing that nanotube formation is always energetically unfavorable. This suggests that the addition of carbon atoms during the CMD reaction favors cap growth over nanotube formation.

REFERENCES

[1] Sumio Iijima, 'Helical microtubules of graphitic carbon', *letters to nature*, vol. 354, pp. 56–58, Nov. 1991

[2] M. Hermesmann and T. E. Müller, 'Green, Turquoise, Blue, or Grey? Environmentally friendly Hydrogen Production in Transforming Energy Systems', May 01, 2022, *Elsevier Ltd*.

[3] F. Ding, A. Rosén, E. E. B. Campbell, L. K. L. Falk, and K. Bolton, *Journal of Physical Chemistry B*, vol. 110, no. 15, pp. 7666–7670, Apr. 2006

[4] Gohier, A., Ewels, C. P., Minea, T. M. & Djouadi, M. A. *Carbon*, vol. 46, pp. 1331–1338, Jul. 2008.

[5] M. Hubert *et al.*, 'DOE Hydrogen Program Record 24005: Clean Hydrogen Production Cost Scenarios with PEM Electrolyzer Technology', 2022

P106: BORONIC ACIDS: A NEW STRATEGY TO BOOST BETA-LACTAM ANTIBIOTICS AS ANTI-TUBERCOLOSIS AGENTS

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ABSTRACT

Tuberculosis (TB) is a highly infectious disease caused by *Mycobacterium tuberculosis* (*Mtb*), one of the most dangerous aerobic bacteria. In 2020 alone, TB was responsible for 1.5 million deaths worldwide, comparable to the 1.8 million deaths caused by COVID-19.[2] The need for **long-term treatments** and the **increase in drug resistance mechanisms** make it necessary to urgently develop new strategies to combat this potentially lethal pathogen.
β-Lactam Antibiotics (BLA) are the most widely used and safest antibiotics in the clinic and include several classes such as penicillins, cephalosporins and carbapenems. However, historically these agents have not been used to treat TB. The main resistance mechanisms to BLA in *Mtb* relies on the expression of BlaC, a specific β-lactamase enzyme capable of hydrolyzing and inactivating the BLA.[3] Recent studies have shown that the combination of meropenem (a β-lactam carbapenem), amoxicillin (a β-lactam penicillin) and clavulanate (a β-lactamase inhibitor) markedly reduced the *Mtb* load in the patient's sputum after two weeks, therefore giving new hope to the use of BLA to tackle the tuberculosis epidemic.[4]
Boronic acid transition state inhibitors (BATSIs) are a class of β-lactamase inhibitors which demonstrated inhibitory activity against several BL enzymes to combat BLA resistance.[4,5] These compounds form a reversible covalent bond between the boron atom and the catalytic serine residue forming a complex with the enzyme which mimic the transition state of the hydrolysis reaction of the BLA, leading to enzyme inactivation and allowing BLA activity restoration.
In the past twenty years, several BATSIs were synthesized by Prof. Prati's group as inhibitors of Serine BL expressed in highly resistant Gram-negative bacteria (*Klebsiella*, *Acinetobacter*, *Pseudomonas*) and some of them proved to inhibit these enzymes in the nanomolar range. The rise of interest on a possible use of BLA against *Mtb* has encouraged our group to investigate whether the BATSI already synthesized, could synergize the activity of a BLA in *Mtb*. Thus, 10 BATSIs were chosen and evaluated as anti-*Mtb* agents against BlaC-producing *Mtb* strains in combination with amoxicillin, a common and low expensive penicillin. Two of these compounds proved to increase amoxicillin susceptibility against BlaC-producing *Mtb* reference strains, encouraging further studies.

REFERENCES

[1] FEMS Microbiol. Rev., 2012, 36(3), 514-32.
[2] https://covid19.who.int.
[3] Antimicrobial agents and chemotherapy, 2006, 50(8), 2762-2771.
[4] ACS infect. Dis., 2015, 1(6), 234-242.
[5] J. Med. Chem., 2023, 66(13), 8510–25.

P107: FLUOROPHOBIC EFFECT ENABLES HIGHLY SENSITIVE PFAS DETECTION IN WATER WITH ELECTROLYTE-GATED ORGANIC TRANSISTORS

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ABSTRACT

PerFluoroAlkyl Substances (PFAS) are a family of chemicals responsible of major environmental pollution worldwide, as they are both persistent and mobile, due to their chemical structure.[1] Environmental control agencies impose strict regulations about PFAS in drinking water, and there is an urgent need for on-field deployable, rapid, reproducible, and inexpensive distributed monitoring of PFAS.[2] In this work we demonstrate an ultra-sensitive sensor for acidic PFAS based on an electrolyte gated organic transistor (EGOT).[3] The sensor is specific thanks to the fluorophobic effect between a perfluorinated mixed SAM and the PFAS in solution, and selective because the electrical response discriminates the change of polarization at the gate electrode proportional to the PFAS chain lengths. We validate the platform using spiked solutions of three model PFAS: i) perfluoro octanoic acid (PFOA), ii) perfluoro hexanoic acid (PFHxA), and iii) perfluoro butanoic acid (PFBA). We assessed the specificity of the sensor using a non-fluorinated surfactant, i.e., sodium dodecyl sulfate (SDS).
We quantify the PFAS in water down to ppt level of detection. Remarkably, our sensing platform discriminates differences in the binding energy as low as 4-5 kJ/mol, which corresponds to a few F…F bonds.

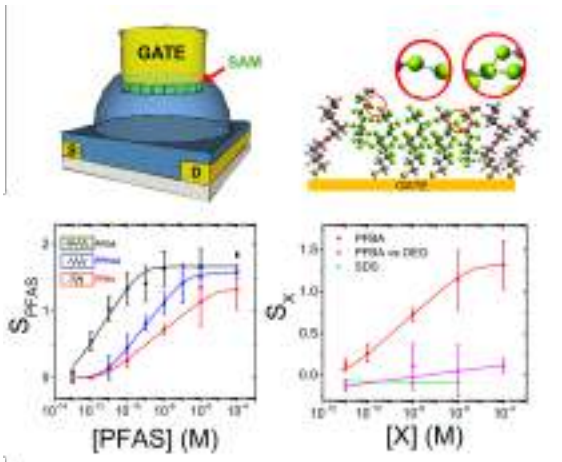

Figure 1. TOP: schematic representation of the EGOT-based sensor and of the mixed SAM. BOTTOM: Dose curves for PFAS detection and control experiments.

REFERENCES

[1] J. P. Giesy, K. Kannan, *Environ. Sci. Technol.* **2001**, *35*, 1339.
[2] A. U. Rehman, M. Crimi, S. Andreescu, *Trends in Environmental Analytical Chemistry* **2023**, *37*, e00198.
[3] R. Zanotti, M. Sensi, M. Berto, A. Paradisi, M. Bianchi, P. Greco, C. A. Bortolotti, M. Di Lauro, F. Biscarini, *Advanced Materials,* **10.1002/adma.202410940.**

P108: GREEN RETROFITTING OF A VINTAGE REACTION: PRODUCTION OF ACETONE FROM RENEWABLE SOURCES VIA PYROLYSIS OF ACETATES

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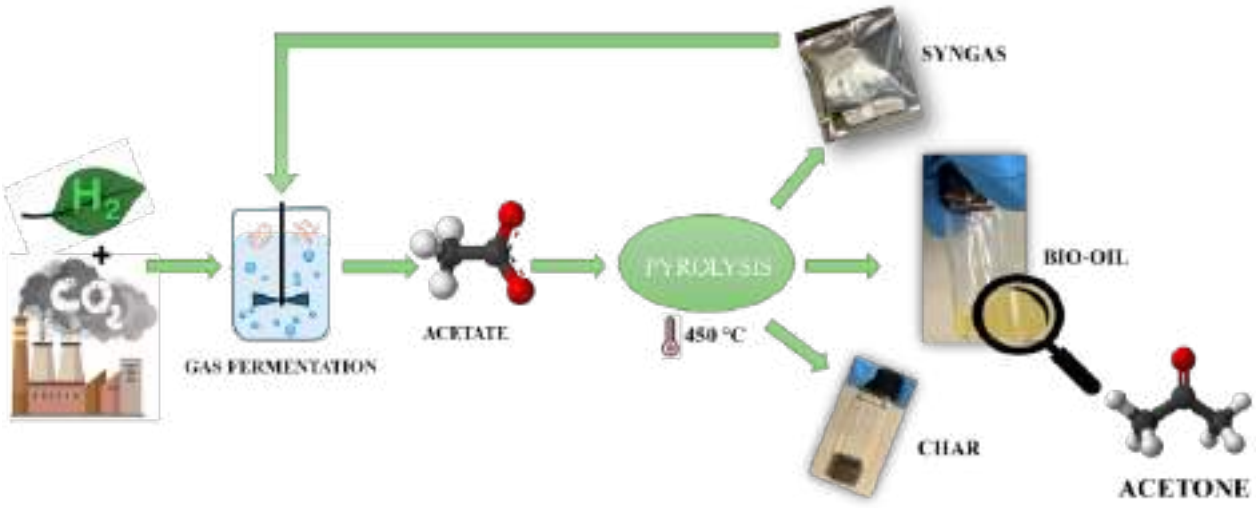
ABSTRACT

CO_2 emissions have exceeded pre-pandemic levels and continue to increase, suggesting a need to develop technologies that can exploit CO2 as a source[1]. There is also a need to decarbonize chemical industries by employing alternative chemical synthesis that are GHG-free sources[2].
The aim of the study was to demonstrate that it is possible to obtain high-purity acetone by the thermal ketonization of acetates resulting from gas fermentation. Acetate is one of the main products of fermentation and anaerobic bioconversion and is the simplest platform chemical that can be generated from CO_2[3].
A series of pyrolysis was performed in a bed fixed reactor system at 450°C using sodium acetate and salts from Carbon Capture and Fixation system (CCF) as feedstock. Pyrolysis was conducted in CO_2 atmosphere and three different retention time were tested. The bio-oil obtained showed an organic content of more than 70%, of which 95% was acetone. Impurities content was negligible and mostly characterised by Isophorone whose quantity did not exceed 1%w/w. Results confirmed pure acetone can be produced from renewable sources.



REFERENCES

[1] Liu, Z.; Deng, Z.; Davis, S.; Ciais, P. Monitoring Global Carbon Emissions in 2022. *Nat Rev Earth Environ* **2023**, *4* (4), 205–206. https://doi.org/10.1038/s43017-023-00406-z.
[2] Dahiru, A. R.; Vuokila, A.; Huuhtanen, M. Recent Development in Power-to-X: Part I - A Review on Techno-Economic Analysis. *Journal of Energy Storage* **2022**, *56*, 105861. https://doi.org/10.1016/j.est.2022.105861.
[3] Mutyala, S.; Kim, J. R. Recent Advances and Challenges in the Bioconversion of Acetate to Value-Added Chemicals. *Bioresource Technology* **2022**, *364*, 128064. https://doi.org/10.1016/j.biortech.2022.128064.

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